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Dated 26 September 2000

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0 E529898-1 D02776
F01/7700 0.00-0009267.6

17 APR 2000

Request for grant of a patent

(See the notes on the back of this form. You can also get an explanatory leaflet from the Patent Office to help you fill in this form)

The Patent Office

Cardiff Road
Newport
Gwent NP9 1RH

1. Your reference	IPD/P2855/1
2. Patent application number *(The Patent Office will fill in this part)*	**0009267.6** 17 APR 2000
3. Full name, address and postcode of the or of each applicant *(underline all surnames)*	THE SECRETARY OF STATE FOR DEFENCE Defence Evaluation and Research Agency Ively Road, Farnborough Hampshire GU14 0LX, UK
Patents ADP number *(if you know it)*	54510014
If the applicant is a corporate body, give the country/state of its incorporation	GB
4. Title of the invention	Novel Compounds
5. Name of your agent *(if you have one)*	Bowdery Anthony Oliver
"Address for service" in the United Kingdom to which all correspondence should be sent *(including the postcode)*	Defence Evaluation & Research Agency IPD (DERA) Formalities A4 Bldg Ively Road Farnborough Hants GU14 0LX United Kingdom
Patents ADP number *(if you know it)*	6935910004

6. If you are declaring priority from one or more earlier patent applications, give the country and the date of filing of the or of each of these earlier applications and *(if you know it)* the or each application number

Country	Priority application number *(if you know it)*	Date of filing *(day / month / year)*
GB	9922179.8	21 September 1999

7. If this application is divided or otherwise derived from an earlier UK application, give the number and the filing date of the earlier application

Number or earlier application	Date of filing *(day / month / year)*

8. Is a statement of inventorship and of right to grant of a patent required in support of this request? *(Answer 'Yes' if:*
a) any applicant named in part 3 is not an inventor, or
b) there is an inventor who is not named as an applicant, or
c) any named applicant is a corporate body.
See note (d))

Yes (b)

Patents Form 1/77

9. Enter the number of sheets for any of the following items you are filing with this form. Do not count copies of the same document

Continuation sheets of this form	-
Description	130
Claim*(s)*	09
Abstract	01
Drawing*(s)*	-

10. If you are also filing any of the following, state how many against each item.

Priority documents	-
Translations of priority documents	-
Statement of inventorship and right to grant of a patent *(Patents Form 7/77)*	-
Request for preliminary examination and search *(Patents Form 9/77)*	-
Request for substantive examination *(Patents Form 10/77)*	-
Any other documents *(please specify)*	-

11. I / We request the grant of a patent on the basis of this application.

Signature F Sedgwick Ms Freda Sedgwick 13 April 2000 Date

12. Name and daytime telephone number of person to contact in the United Kingdom — Maria T. Burkes 01252 392561

Warning

After an application for a patent has been filed, the Comptroller of the Patent Office will consider whether publication or communication of the invention should be prohibited or restricted under Section 22 of the Patents Act 1977. You will be informed if it is necessary to prohibit or restrict your invention in this way. Furthermore, if you live in the United Kingdom, Section 23 of the Patents Act 1977 stops you from applying for a patent abroad without first getting written permission from the Patent Office unless an application has been filed at least 6 weeks beforehand in the United Kingdom for a patent of the same invention and either no direction prohibiting publication or communication has been given, or any such direction has been revoked.

Notes

a) If you need help to fill in this form or have any questions, please contact the Patent Office on 0645 500505.

b) Write your answers in capital letters using black ink or you may type them.

c) If there is not enough space for all the relevant details on any part of this form, please continue on a separate sheet of paper and write "see continuation sheet" in the relevant part(s). Any continuation sheet should be attached to this form.

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Novel Compounds

The present invention relates to novel compounds having a fused heterocyclic ring which have the properties of liquid crystals, together with processes for their preparation and liquid crystal devices incorporating them.

The term "liquid crystals" is well known. It refers to compounds which, as a result of their structure, will align themselves in a similar orientation, preferably at working temperatures, for example of from -40 to 200°C. These materials are useful in various devices, in particular the liquid crystal display devices or LCDs.

Liquid crystals can exist in various phases. In essence there are three different classes of liquid crystalline material, each possessing a characteristic molecular arrangement. These classes are nematic, chiral nematic (cholesteric) and smectic.

Broadly speaking, the molecules of nematic compounds will align themselves in a particular orientation in a bulk material. Smectic materials, in addition to being orientated in a similar way, will align themselves closely in layers.

A wide range of smectic phases exists, for example smectic A and smectic C. In the former, the molecules are aligned perpendicularly to a base or support, whilst in the latter, molecules may be inclined to the support. Some liquid crystal materials possess a number of liquid crystal phases on varying the temperature. Others have just one phase. For example, a liquid crystal material may show the following phases on being cooled from the isotropic phase:- isotropic - nematic - smectic A - smectic C - solid. If a material is described as being smectic A then it means that the material possesses a smectic A phase over a useful working temperature range.

Such materials are useful, in particular in display devices where their ability to align themselves and to change their alignment under the influence of voltage, is used to impact on the path of polarised light, thus giving rise to liquid crystal displays. These are widely used in devices such as watches, calculators, display boards or hoardings, computer screens, in particular laptop computer screens etc. The properties of the compounds which impact on the speed with which the compounds respond to voltage charges include molecule size, viscosity (Δn), dipole moments ($\Delta\varepsilon$), conductivity etc.

The applicants have found a new class of chemicals which have useful liquid crystal properties. In particular the invention provides a liquid crystal compound having a fused five and six-membered ring, at least one of said rings containing a heteroatom, and at least one of said rings carrying a substitutent. Preferably, each ring has at least one substitutent.

Suitable heteroatoms for use in the ring system of the invention include oxygen, sulphur, nitrogen and selenium. Where nitrogen is present, it may carry a hydrogen or a substituent group, depending upon the nature and the aromaticity of the ring system.

The ring system may be aromatic or non-aromatic, but is preferably aromatic.

Specific examples of the ring system of the invention include benzofurans and benzopyrans.

The nature of the substituents on the ring will determine the particular liquid crystal properties of the compound. Large substituents will tend to increase the viscosity of the compound, thereby increasing the time taken for the molecules to adopt the appropriate orientation under the influence of a

voltage. The number of free electrons which are contained within the substitutents influences optical properties of the compound. Aromatic rings will have relatively high conductivity whereas strongly electronegative groups such as cyano, will tend to reduce conductivity.

The nature of the substitutents on the ring can therefore be selected so as to impart the desired liquid crystal properties on the final compound. For example, some applications as outlined below require chiral molecules. For this purpose, the compounds of the invention suitably contain an asymmetric centre.

Typical substituents will comprise a functional group, optionally substituted hydrocarbyl, optionally substituted alkoxy, optionally substituted heterocyclyl or carboxy or a hydrocarbyl ester or amide thereof.

As used herein, the term "hydrocarbyl" refers to any structure comprising carbon and hydrogen atoms. For example, these may be alkyl, alkenyl, alkynyl, aryl such as phenyl or napthyl, arylalkyl, cycloalkyl, cycloalkenyl or cycloalkynyl. Suitably they will contain up to 20 and preferably up to 10 carbon atoms. The term "heterocyclyl" includes aromatic or non-aromatic rings, for example containing from 4 to 20, suitably from 5 to 10 ring atoms, at least one of which is a heteroatom such as oxygen, sulphur or nitrogen. Examples of such groups include furyl, thienyl, pyrrolyl, pyrrolidinyl, imidazolyl, triazolyl, thiazolyl, tetrazolyl, oxazolyl, isoxazolyl, pyrazolyl, pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, triazinyl, quinolinyl, iosquinolinyl, quinoxalinyl, benzthiazolyl, benzoxazolyl, benzothienyl or benzofuryl.

As used herein, the term "alkyl" refers to straight or branched chain alkyl groups, suitably containing up to 20 and preferably up to 6 carbon atoms, and the term "alkoxy" relates to -O-alkyl

groups. The term "alkenyl" and "alkynyl" refer to unsaturated straight or branched chains which include for example from 2-20 carbon atoms, for example from 2 to 6 carbon atoms. In addition, the term "aryl" refers to aromatic groups such as phenyl or naphthyl. The terms "cycloalkyl", "cycloalkenyl" and "cycloalkynyl" refer to such groups which are cyclic and have at least 3 and suitably from 5 to 20 ring atoms. These rings may be fused together to form bicyclic, tricyclic or even larger multiple ring systems.

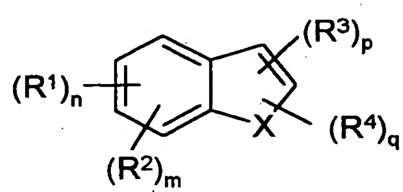
Optionally subsituted hydrocarbyl groups will be may be substituted by functional groups, or by other types of hydrocarbyl group. For example, cyclic groups such as aryl, heterocyclic or cycloalkyl, cycloakenyl or cycloalkynyl may be substituted by hydrocarbyl chains such as alkyl, alkenyl or alkynyl groups as well as functional groups. Where the hydrocarbyl group itself an alkyl, alkenyl or alkynyl group, it may be substituted with cylic groups as described above, which may themselves be further substituted by hydrocarbyl or functional groups.

The term "functional group" refers to reactive groups such as halo, cyano, nitro, oxo, $C(O)_nR^a$, OR^a, $S(O)_tR^a$, NR^bR^c, $OC(O)NR^bR^c$, $C(O)NR^bR^c$, $OC(O)NR^bR^c$, $-NR^7C(O)_nR^6$, $-NR^aCONR^bR^c$, $-C=NOR^a$, $-N=CR^bR^c$, $S(O)_tNR^bR^c$ or $-NR^bS(O)_tR^a$ where R^a , R^b and R^c are independently selected from hydrogen or optionally substituted hydrocarbyl, or R^b and R^c together form an optionally substituted ring which optionally contains further heteroatoms such as $S(O)_s$, oxygen and nitrogen, t is an integer of 1 or 2, t is 0 or an integer of 1-3.

The term "heteroatom" as used herein refers to non-carbon atoms such as oxygen, nitrogen, selenium or sulphur atoms as mentioned above. Where the nitrogen atoms are present, they will generally be present as part of an amino residue so that they will be substituted for example by hydrogen or alkyl.

The term "amide" is generally understood to refer to a group of formula $C(O)NR^aR^b$ where R^a and R^b are hydrogen or an optionally substituted hydrocarbyl group.

In particular, the compounds of the invention are liquid crystal compounds of general formula (I)



(I)

where X is O, S or Se,
each R^1 and R^3 are independently selected from cyano, halo, optionally substituted hydrocarbyl, optionally substituted alkoxy, optionally substituted heterocyclyl or carboxy or a hydrocarbyl ester or amide thereof, provided that at least one or group R^1 or R^3 is other than cyano or halo,
each R^2 and R^4 is independently selected from halo, nitro, lower alkyl optionally substituted by halo, or a group $R^aC(O)O-$ where R^a is optionally substituted hydrocarbyl,
n is 1 or 2, m is 0, 1, 2 or 3, p is 1 or 2 and q is 0 or 1, provided n + m do not exceed 4 and p = q do not exceed 2, provided the compounds are other than those described in DE1990517 or WO 98/04544.

Preferably, in the compound of formula (I), n is 1, and m is 0, 1 or 2, and more preferably 0 or 1 and most preferably 0.

Preferably p is 1 and q is 0.
Suitable lower alkyl groups for R^2 and R^4 include methyl, fluoromethyl or trifluoromethyl.

Preferably, any group R^2 or R^4 which are present are halo, especially fluoro.

Where R^2 or R^4 are groups of formula $R^aC(O)O-$, R^a is suitably alkyl or aryl.

In a particularly preferred embodiment, one of R^1 or R^3 is cyano or halo and the other is optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, an optionally substituted aryl, optionally substituted heterocyclyl, carboxy or an ester thereof
Preferably X is oxygen.

Suitably R^1 and R^3, when they are other than cyano or halo, are selected from optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, an optionally substituted aryl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl or optionally substituted cycloalkynyl.

Suitable optional substituents for alkyl, alkenyl, alkynyl, groups R^1 and R^3 include functional groups as defined above, as well as aryl, cycloalkyl, heterocyclyl any of which may be substituted by alkyl, alkenyl or alkynyl as well as functional groups as defined above.

Suitable optional substituents for aryl, heterocyclyl, cycloalkyl, cycloalkenyl or cycloalkynyl groups R^1 and R^3 include those listed above in respect of alkyl, alkyenyl and alkynyl groups, as well as alkyl, alkenyl or alkynyl, any of which may be optionally subsituted by a functional group, an aryl group, a heterocyclic group or a cycloalkyl, cycloalkenyl or cycloalkynyl group.

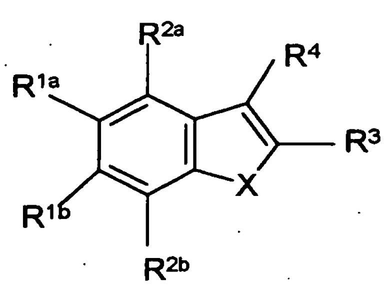
Preferably, R^1 and R^3, where these are other than cyano or halo, are selected from optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, an optionally substituted aryl, optionally substituted heterocyclyl, carboxy or a hydrocarbyl ester thereof.

Where these are carboxy ester groups, they are preferably alkyl esters or aryl esters such as phenyl esters where the phenyl group may be optionally substituted for example with alkyl, alkoxy or cyano groups.

A particularly preferred group for R^1 or R^3 where these are other than cyano or halo are optionally substituted phenyl. Particularly suitable substituents include alkyl especially C_{3-9}alkyl, alkoxy such as C_{3-9}alkoxy, cyano or phenyl which may itself be substituted by alkyl or cyano.

Suitably substituents are arranged on the ring so as to confer an advantageous dipole on the compound. For this purpose, the substituents are suitably arranged such that the overall shape of the molecule is either bent or wedge shaped. Thus substituents are suitably positioned at the 2 and 6 positions of the bicyclic ring where the group X is at position 1.

In particular, the invention provides a compound of general formula (IA)



(IA)

where X is as defined in claim 1, R^{1a} and R^{1b} are independently selected from hydrogen, cyano, halo, optionally substituted hydrocarbyl, optionally substituted heterocyclyl or carboxy or a hydrocarbyl ester or amide thereof, provided that at least one group R^{1a} or R^{1b} is other than hydrogen;
one of R^3 or R^4 is cyano, halo, optionally substituted hydrocarbyl, optionally substituted heterocyclyl or carboxy or a hydrocarbyl ester or amide thereof, and the other is hydrogen, halo, nitro, lower alkyl optionally substituted by halo, or a group $R^aC(O)O-$ where R^a is optionally substituted hydrocarbyl;
R^{2a} and R^{2b} are independently selected from hydrogen, halo, nitro, lower alkyl optionally substituted by halo, or a group $R^bC(O)O-$ where R^b is optionally substituted hydrocarbyl.

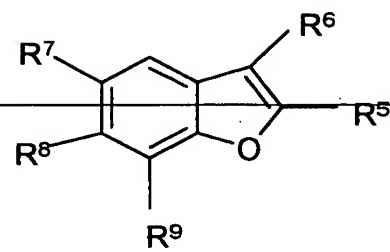
subject to the further provisos that:
(i) at least one group R^{1a} or R^{1b} or R^3 or R^4 is other than cyano or halo;
(ii) where X is S, R^3 is carboxy or a hydrocarbyl ester or amide thereof, R^4 is hydrogen, R^{2a} and R^{2b} are not both fluoro;
(iii) where X is O, R^1 is an optionally substituted hydrocarbyl or carboxy or a hydrocarbyl ester or amide thereof, R^2 is hydrogen, and R^{1b} and R^{2b} are both fluorine, then R^3 is other than C_{1-8} alkyl.

Preferably in the compound of formula (IA) R^{2a} is hydrogen.

Suitably at least one of R^{1b}, R^{2b} or R^4 in formula (IA) is fluoro.

Preferably one of R^{1b} or R^{1a} or R^3 or R^4 in formula (IA) is cyano or halo and the other is optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, an optionally substituted aryl, optionally substituted heterocyclyl, carboxy or a hydrocarbyl ester thereof.

A particularly preferred group of compounds of the invention are of formula (II)



(II)

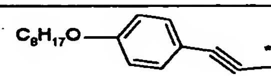
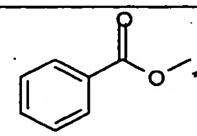
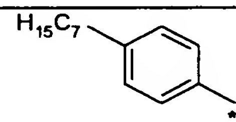
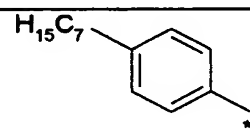
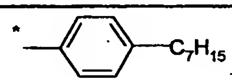
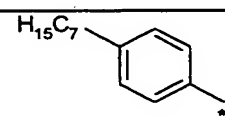
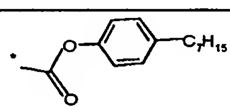
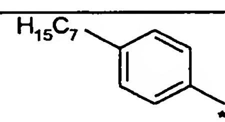
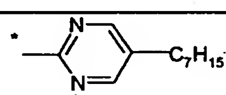
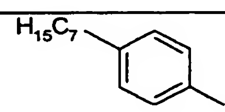
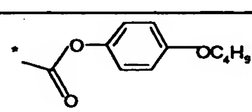
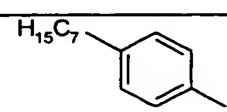
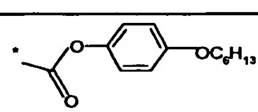
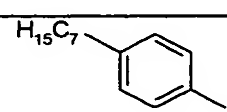
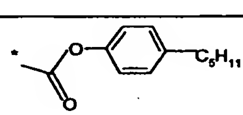
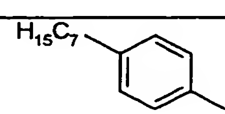
wherein R^5 is a group R^3 as defined above in relation to formula (I),
one of R^7 and R^8 is a group R^1 as defined in relation to formula (I) and the other is hydrogen or a group R^1 as defined in relation to formula (I);
R^6 is hydrogen or fluoro, and
R^9 is hydrogen or fluoro,
provided that where R^5 is cyano or fluoro, at least one of R^7 or R^8 is optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally subsituted alkoxy, optionally substituted aryl, optionally substituted heterocyclyl, carboxy or an ester thereof; and where one of R^7 or R^8 is cyano or fluoro and the other is hydrogen, R^5 is optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted alkoxy, optionally substituted aryl, optionally substituted heterocyclyl, carboxy or an ester thereof.

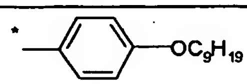
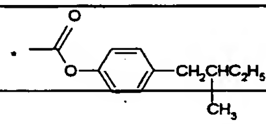
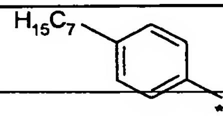
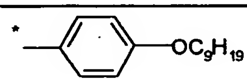
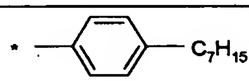
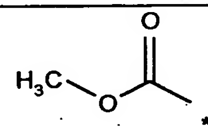
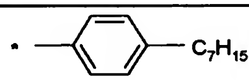
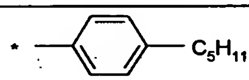
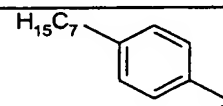
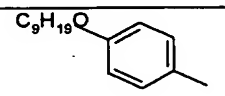
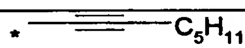
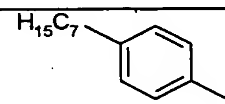
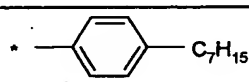
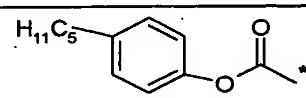
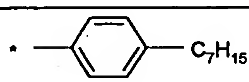
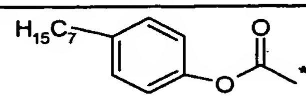
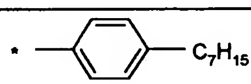
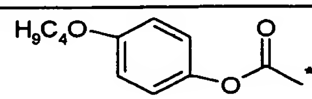
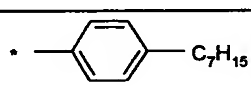
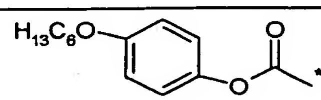
Preferred substituents for R^5 and R^7 and/or R^8 include cyano; fluoro; alkoxy; alkenyl; alkyl, aryl or alkylaryl esters of carboxy; arylalkyl, alkenylaryl wherein the aryl ring is optionally substituted with an alkyl group, a functional group such as fluoro or alkoxy, or further aryl groups which are themselves optionally substituted with alkyl; optionally

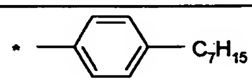
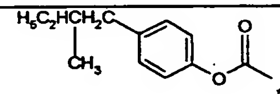
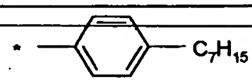
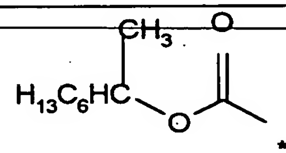
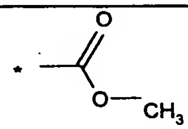
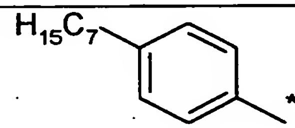
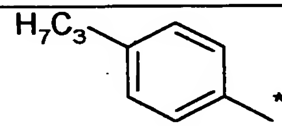
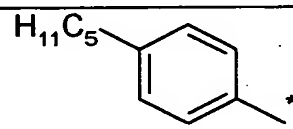
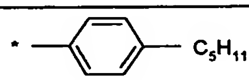
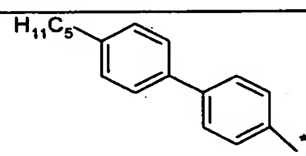
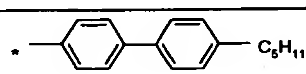
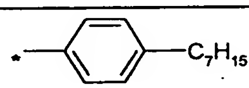
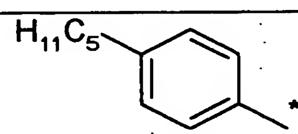
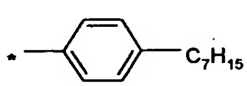
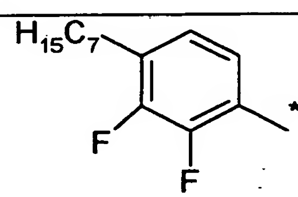
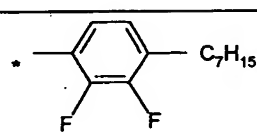
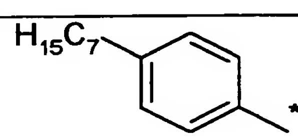
substituted pyrimidinyl wherein the optional substituents are in particular alkyl.

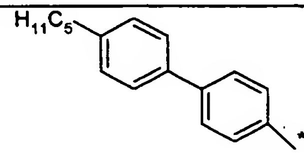
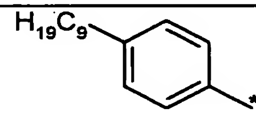
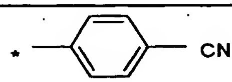
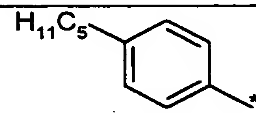
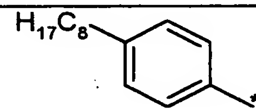
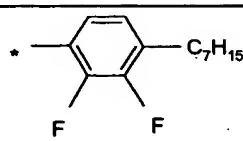
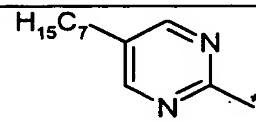
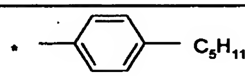
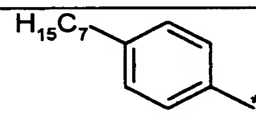
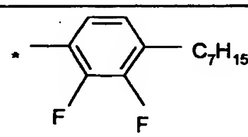
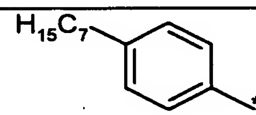
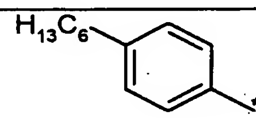
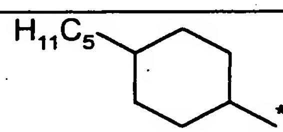
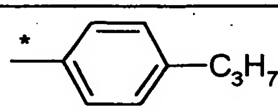
Particular examples of the compounds of formula (II) are listed in Table 1.

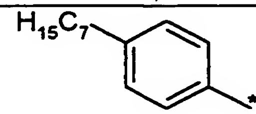
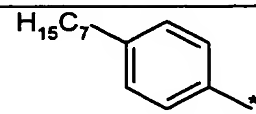
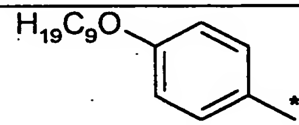
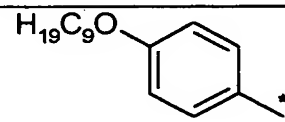
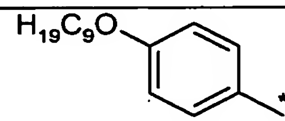
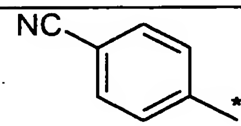
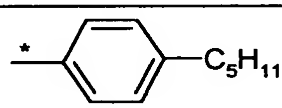
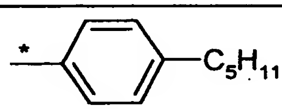
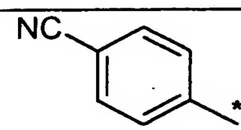
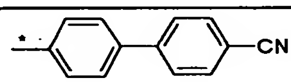
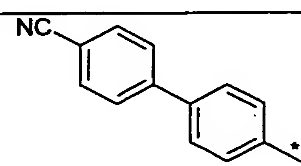
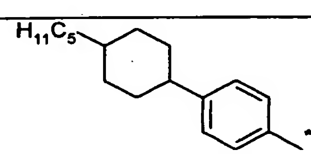
Table 1

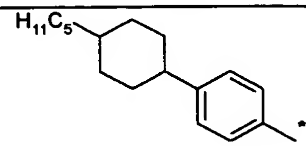
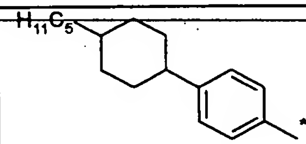
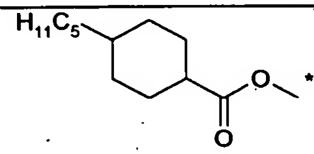
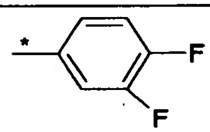
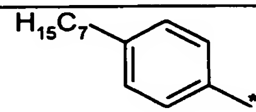
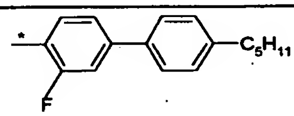
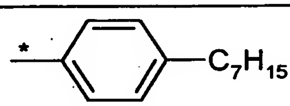
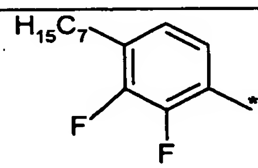
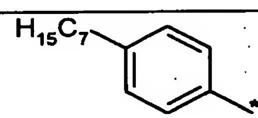
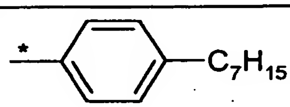
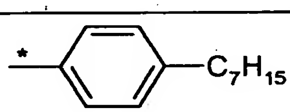
Comp No.	R^5	R^6	R^7	R^8	R^9
1	$-OC_8H_{17}$	H			H
2	$-CO_2C_2H_5$	H		H	H
3	CN	H		H	H
4		H		H	H
5		H		H	H
6		H		H	H
7		H		H	H
8		H		H	H
9		H		H	H

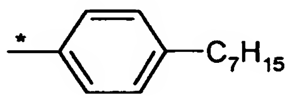
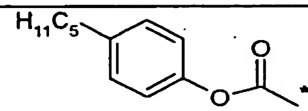
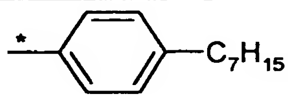
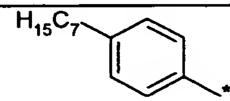
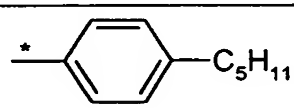
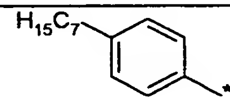
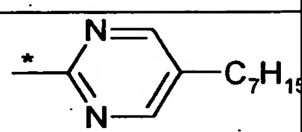
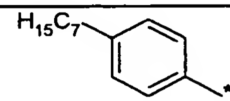
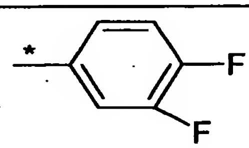
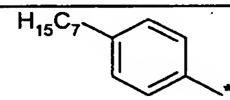
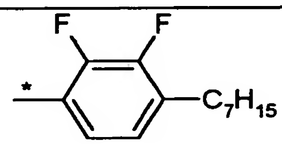
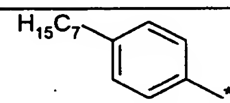
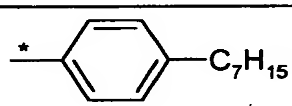
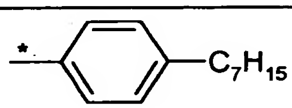
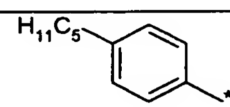
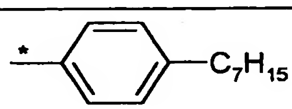
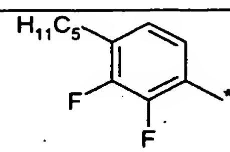
Comp No.	R^5	R^6	R^7	R^8	R^9
10		H	CO_2CH_3	H	H
11		H		H	H
12		H	CN	H	H
13		H		H	H
14		H	CN	H	H
15		H		H	H
16	CN	H		H	H
17		H		H	H
18		H		H	H
19		H		H	H
20		H		H	H
21		H		H	H

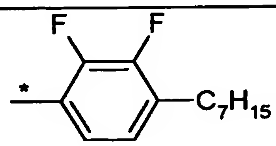
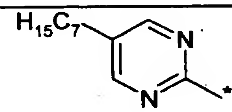
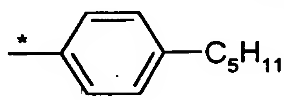
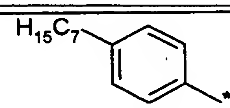
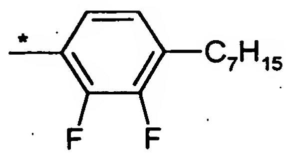
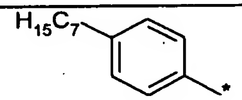
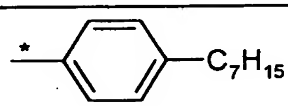
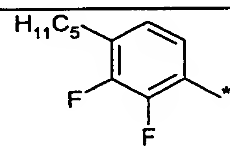
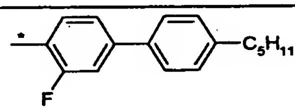
Comp No.	R^5	R^6	R^7	R^8	R^9
22		H		H	H
23		H		H	H
24		H		H	H
25	CN	H		H	H
26	CN	H		H	H
27		H	CN	H	H
28	CN	H		H	H
29		H	CN	H	H
30		H		H	H
31		H		H	H
32		H		H	H

Comp No.	R^5	R^6	R^7	R^8	R^9
33	C_7H_{15}	H		H	H
34	CN	H		H	H
35		H		H	H
36	CN	H		H	H
37		H		H	H
38		H		F	F
39		H		F	F
40	CN	H		H	H
41	CN	H		H	H
42		H	CN	H	H

Comp No.	R^5	R^6	R^7	R^8	R^9
43	CO_2H	H		H	H
44	$CONH_2$	H		H	H
45	CO_2CH_3	H		H	H
46	CO_2H	H		H	H
47	$CONH_2$	H		H	H
48	C_7H_{15}	H		H	H
49		H	Br	H	H
50		H		H	H
51		H	C_5H_{11}	H	H
52	C_5H_{11}	H		H	H
53	CO_2H	H		H	H

Comp No.	R^5	R^6	R^7	R^8	R^9
54	$CONH_2$	H		H	H
55	CN	H		H	H
56	CN	H		H	H
57		H		H	H
58		H	C_7H_{15}	F	F
59		H		F	F
60	C_7H_{15}	H	$C_2H_5OC(O)-$	H	H
61	C_7H_{15}	H	$H_{11}C_5C{\equiv}C-$	H	H
62	$-C(O)OCH(CH_3)C_6H_{13}$	H		H	H
63		H	CO_2H	H	H
64		H	$CO_2CH_2CH_3$	H	H

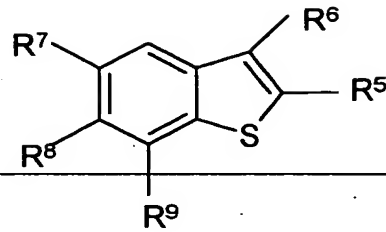
Comp No.	R^5	R^6	R^7	R^8	R^9
65		H		H	H
66		H		H	H
67		H		H	H
68		H		H	H
69		H		H	H
70		H		H	H
71		H	$-C{\equiv}C-C_5H_{11}$	H	H
72		H		H	H
73		H		H	H

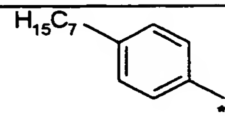
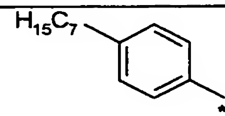
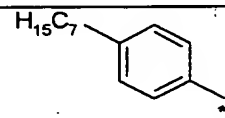
Comp No.	R^5	R^6	R^7	R^8	R^9
74		H		H	H
75		H		H	H
76		H		H	H
77		H		F	F
78		H	C_7H_{15}	F	F

In the above Table, * indicates the point of attachment to the ring structure.

Particular examples of compounds of formula (I) where X is sulphur are listed in Table 2.

Table 2

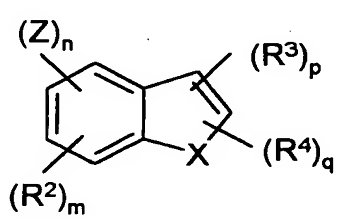


Comp No.	R^5	R^6	R^7	R^8	R^9
100	$-CO_2H$	H		H	H
101	$-CONH_2$	H		H	H
102	CN	H		H	H

The compounds of the invention may be prepared by conventional methods which would be apparent to a skilled chemist.

In particular, compounds may be prepared by adding substituents to a bicyclic ring.

Thus, for example, a compound of formula (I) can be prepared by reacting a compound of formula (III)



(III)

where R^2, R^3, R^4, X, n, m, p and q are as defined in relation to formula (I), and Z is either a leaving group or a group $B(OH)_2$, with a compound of formula (IV)

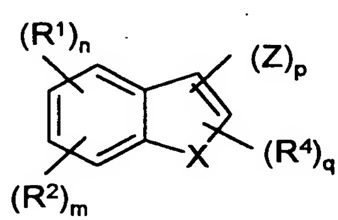
$$R^1\text{-}Z'$$

(IV)

where R^1 is as defined in relation to formula (I) and Z' is a group $B(OH)_2$ where Z is a leaving group, or a leaving group where Z is a group $B(OH)_2$;
and thereafter if desired or necessary, converting a group R^2, R^3 or R^4 to a different such group.

Suitable leaving groups for Z or Z' include halo such as bromo or iodo, mesylate, tosylate and triflate. The reaction is suitably effected in an inert organic solvent, such as 1,2-dimethoxyethane in the presence of a base such as sodium or potassium carbonate. The reaction is suitably effected in the presence of an inert atmosphere such as a nitrogen atmosphere. Optionally a catalyst such as a palladium catalyst for example tetrakis (triphenylphosphine) palladium is present. The reaction is suitably effected at elevated temperatures, for instance at the reflux temperature of the solvent.

Of course, other substituents may be introduced in an analogous way and the order in which this is done will depend to a large extent on the nature of the substituents and where they are positioned on the ring. In an alternative route, for example, compounds of formula (I), are prepared by reacting a compound of formula (V)



(V)

where R^1, R^2, R^4, X, n, m, p and q are as defined in relation to formula (I), and Z is as defined in relation to formula (III), with a compound of formula (VI)

$$R^3\text{-}Z'$$

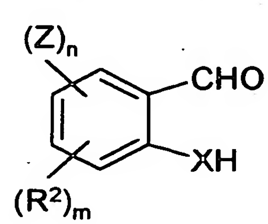
(VI)

where R^3 is as defined in relation to formula (I) and Z′ is as defined in relation to formula (IV), and thereafter, if necessary, changing any groups R^1, R^2 and R^4 to different such groups.

Suitable leaving groups Z or Z′ and reaction conditions will be similar to those described above in relation to the reaction between compounds of formula (III) and (IV).

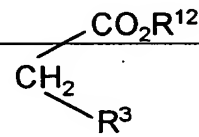
The conversion of groups R^1, R^2, R^3 and R^4 to different such groups could be carried out by conventional methods as would be apparent to a skilled chemist. A particularly useful reaction in this context is the conversion of a carboxylic ester group such as an alkyl ester, in particular an ethyl ester, to a cyano group. This reaction may be achieved by hydrolysis of the carboxylic ester group, followed by conversion of the resultant carboxylic acid to the corresponding acid chloride and thereafter to the amide. Dehydration of the amide gives the cyano compound. Each of the steps can be carried out using conventional chemistry and these are illustrated in the Examples given hereinafter.

Compounds of formula (III) and (V) are suitably prepared by a cyclisation reaction as would be understood in the art. For example, a compound of formula (III) might be prepared by reacting a compound of formula (VII)



(VII)

where X, n and m are as defined in relation to formula (I), and Z is as defined in relation to formula (III), with a compound of formula (VIII)



(VIII)

where R^3 is as defined above in relation to formula (I) and R^{12} is an alkyl group such as ethyl. Thereafter, groups R^3 can be changed to different such groups on the compound of formula (III) in a similar manner to that outlined above.

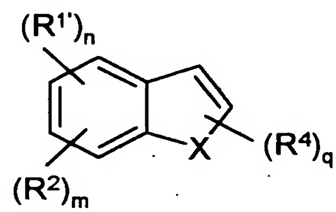
A particular preferred compound of formula (VIII) is a compound where R^3 is a carboxylic ester group such as an alkyl ester group as this gives rise to the possibility of subsequent modification as outlined above. Thus a suitable compound of formula (VIII) is diethyl bromomalonate.

The reaction is suitably effected in an organic solvent such as butanone in the presence of a base such as potassium carbonate.

Compounds of formulae (IV) and (VI) are either known compounds or they can be prepared by conventional methods. For example where Z or Z′ are $B(OH)_2$ groups, these may be prepared by reacting the corresponding halo substituted compounds with magnesium in an organic solvent such as tetrahydrofuran, then with trimethyl borate, and finally acidifying the product using a mineral acid such as hydrochloric acid. Examples of such preparations are illustrated hereinafter.

Compounds of formula (XI) and (XII) are either known compounds or they can be prepared from known compounds by conventional methods.

In an alternative approach, compounds of formula (I) where q is 0 and p is 1 and R^3 is a carboxy group may be prepared by introduction of a substituent R^3 group to a compound of formula (IX)



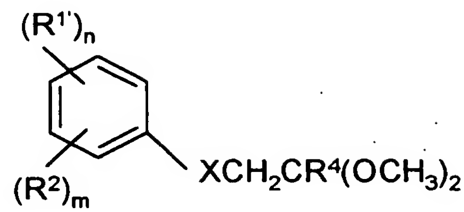
(IX)

were R^2, R^4, X, m,n and q are as defined in relation to formula (I), and $R^{1'}$ is a group R^1 as defined in relation to formula (I) or a precursor thereof; with a carboxylating agent such as Cardice in the presence of a base such as n-butyllithium and an organic solvent such as tetrahydrofuran, and thereafter acidifying the product with an acid such as glacial acetic acid. The carboxy group can subsequently be converted into different R^3 groups as required.

Suitable precursor groups $R^{1'}$ include groups which can be converted to the desired R^1 groups by conventional chemistry. Thus an example of such a group would be a group Z or Z′ as defined above.

Compounds of formula (IX) where $R^{1'}$ is a group R^1 (hereinafter referred to as compounds of formula (IXA) may have liquid crystal properties in their own right and therefore these form a further aspect of the invention.

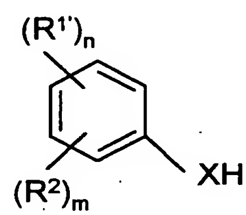
Compounds of formula (IX) where q is 0 may be prepared by cyclisation of an acetal compound of formula (X)



(X)

where R^2, R^4 X, n and m are as defined in relation to formula (I), and $R^{1'}$ is as defined in relation to formula (IX); in the presence of polyphosphoric acid. The reaction is suitably effected in an organic solvent such as chlorobenzene at elevated temperature, for example at the reflux temperature of the solvent.

Compounds of formula (X) are suitably prepared by reacting a compound of formula (XI)



(XI)

where $R^{1'}$, R^2, X, m and n are as defined above, with a compound of formula (XII)

$$Z''-CH_2CR^4(OCH_3)_2$$

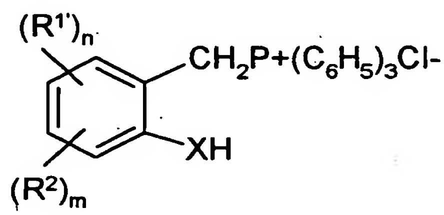
(XII)

where R^4 is as defined in relation to formula (I) and Z″ is a leaving group. Suitable leaving groups Z″ are defined above in relation to the group Z. The reaction is suitably effected in the presence of a base such as potassium carbonate in an organic solvent such as butanone.

Compounds of formula (IX) may be converted to compounds of formula (V) where Z is a $B(OH)_2$ group by reaction with

trimethyl borate in the presence of a base such as n-butyl lithium. Subsequent acidification with an acid such as hydrochloric acid will yield the desired product. The reaction is suitably effected in an organic solvent such as tetrahydrofuran and reactions of this type are exemplified hereinafter.

An alternative cyclisation route which can lead directly to compounds of formula (I) where q is 0 involves reaction of a compound of formula (XIII)



(XIII)

where $R^{1'}$, R^2, X, n and m are as defined above, with a compound of formula (XIV)

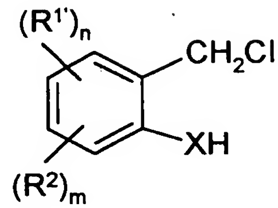
$$HO_2C-R^{3'}$$

(XIV)

where $R^{3'}$ is a group R^3 as defined in relation to formula (I)or a precursor thereof. The reaction is suitably effected in an organic solvent such as dichloromethane in the presence of a base such as N,N'-dicyclocarbodiimide (DCC) and 4-N,N-dimethylaminopyridine (DMAP). The reaction is suitably carried out under an inert atmosphere for example of nitrogen.

Precursor groups $R^{3'}$ may be similar to those defined above in relation to $R^{1'}$.

Compounds of formula (XIII) may be derived from compounds of formula (XIV)



(XIV)

where $R^{1'}$, R^2, X, n and m are as defined above with triphenylphosphine under conditions such as those illustrated hereinafter.

Variations and modifications to these routes would be apparent to the skilled person and these are all encompassed by the invention.

The compounds of the invention can be selected such that their liquid crystal properties, in particular the nematic/smectic properties, suit the desired application. This may be achieved by varying the substituent groups on the central ring structure as outlined above, or it may be effected by mixing the compounds with other compounds of the invention or other different liquid crystal compounds. Mixtures are suitably eutectic mixtures. The compounds of the present invention may be mixed with each other to form useful liquid crystal mixtures, they may also be used with liquid crystal polymers or other low molar mass non-polymer liquid crystal materials.

As would be appreciated, the compounds of the invention can be used in a wide variety of devices, depending upon their particular properties. For applications where nematic compounds are required, compounds with low melting points, high transition temperatures (TN-I(°C)), low viscosity and high dipole moments giving for example high values of ($\Delta\varepsilon$) are required. Compounds of the invention include those which have such properties and other properties such as flexoelectric

properties. Where the melting point is not sufficiently low, this may be reduced by mixing the compound of the invention with other liquid crystal compounds, in particular a different compound of the invention, so as to form a mixture, preferably a eutectic mixture.

Transition temperatures may be increased by using or including in the mixture compounds of the invention which comprise at least three carbocyclic, heterocyclic or aryl ring systems, for example, compounds of formula (I) where both R^1 and R^3 comprise a carbocyclic, heterocyclic or aryl group.

For trifluoroterphenyl (TFT) devices, compounds of the invention with TN twisted nematic values of the order of 90° are suitably selected. This is indicative of the degree of twist present in the alignment of the molecules. The viscosity of such compounds (Δn) is suitably low and for this reason, compounds with saturated substituent groups may be preferred. The compounds should have a positive $\Delta\varepsilon$, which is a result of a longitudinal dipole moment. The value of the elastic constants ratio, K_{11}/K_{33}, is preferably high, whilst the conductivity is preferably low. In order to achieve these latter requirements, halo substituents such as fluoro may be preferred to cyano substituents.

Compounds of the invention may have the properties of the so called "super-twist nematics" where the TN values are of the order of 240-270°. Such compounds generally have a high Δn value, and so may contain aromatic rings. They will have a positive $\Delta\varepsilon$ and the value of K_{11}/K_{33} is high to provide a sharp threshold.

Liquid crystal devices comprising compounds of the invention of mixtures form a further aspect of the invention. Examples of such devices include optical and electro-optical devices, magneto-optical devices and devices providing responses to

stimuli such as temperature changes and total or partial pressure changes. The compounds described above may also be included in a mixture, where the mixture comprises at least two compounds. Typical mixtures include mixtures consisting of compounds of the above-described compounds and also mixtures comprising at least one compound as described and at least one different liquid crystal compound.

When a smectic A phase compound of the invention is composed of chiral molecules, it may exhibit an electroclinic effect, i.e. a direct coupling of molecular tilt to applied field. The origin of the electroclinic effect in a smectic A phase composed of chiral polar molecules has been described by Garoff and Meyer as follows. The application of an electric field parallel to the smectic layers of such a smectic A phase biases the free rotation of the transverse molecular dipoles and therefore produces a non-zero average of the transverse component of the molecular polarisation. When such a dipole moment is present and coupled to the molecular chirality, a tilt of the long molecular axis (the director) is induced in a plane perpendicular to the dipole moment.

In thin samples, for example 1-3μm, and with the smectic layers tilted or perpendicular with respect to the glass plates the electroclinic effect is detectable at low applied fields.

In an aligned smectic A sample a tilt of the director is directly related to a tilt of the optic axis. The electroclinic effect results in a linear electro-optic response. The electro-optic effect can manifest itself as a modulation of the effective birefringence of the device.

Electroclinic (EC) devices are useful, for example, in spatial light modulators having an output that varies linearly with applied voltage. A further advantage of EC devices is that they have high speed response times, much faster than twisted nematic

type devices. One known type of ferroelectric device is bistable, in contrast the EC device is not bistable and has an output that varies linearly with applied voltage.

The electroclinic effect is sometimes referred to as the soft-mode effect see G Andersson et al in Appl. Phys. Lett., 51, 9, (1987).

In general terms, regarding the electroclinic effect, it is advantageous if on applying a small voltage there results a large induced tilt. An increase in induced tilt may result in an increase in contrast ratio. It is also advantageous if a large induced tilt can be obtained at as low a voltage as possible.

It is also advantageous if the relationship between molecular induced tilt and applied voltage is temperature independent. When an increase in applied voltage results in little or no change in induced tilt then the material being tested is generally referred to as exhibiting a saturation voltage effect.

There are a variety of electroclinic devices in which the compounds of the present invention may be incorporated. For example, in a liquid crystal cell active black plane driving may be utilised. One of the walls forming the cell may be formed from a silicon substrate e.g. a wafer which possesses circuitry for driving pixels.

For many of these devices there exists an optimum thickness for the cell which is related to the birefringence (Δ n) given by:

$$d = \frac{(2m+1)\lambda}{4(\Delta n)}$$

wherein λ = wavelength of operation

Δn = birefringence of liquid crystalline material

m = integer.

Some suitable methods for driving electroclinic devices described by the present invention may be found in UK patent application GB-2 247 972 A.

The mode of operation of these devices includes either amplitude modulation or phase modulation. Similarly devices may be used in reflectance or transmissive mode.

By S_A* is meant a S_A phase which contains some proportion of chiral molecules, and therefore it is preferable that the compounds of the invention used in this way are chiral.

Cholesteric or chiral nematic liquid crystals possess a twisted helical structure which is capable of responding to a temperature change through a change in the helical pitch length. Therefore as the temperature is changed, then the wavelength of the light reflected from the planar cholesteric structure will change and if the reflected light covers the visible range then distinct changes in colour occur as the temperature varies. This means that there are many possible applications including the areas of thermography and thermooptics.

The cholesteric mesophase differs from the nematic phase in that in the cholesteric phase the director is not constant in space but undergoes a helical distortion. The pitch length for the helix is a measure of the distance for the director to turn through 360°.

By definition, a cholesteric material is chiral material. Chiral compounds of the invention may exhibit a helical mesophase and so may be used in thermographic or thermooptic applications. Chiral compounds of the invention may also be used in electro-

optical displays as dopants, for example in twisted nematic displays where they may be used to remove reverse twist defects. They may also be used in cholesteric to nematic dyed phase change displays where they may be used to enhance contrast by preventing wave-guiding.

Thermochromic applications of cholesteric liquid crystal materials usually use thin film preparations of the materials which are then viewed against a black background. These temperature sensing devices may be placed into a number of applications involving thermometry, medical thermography, non-destructive testing, radiation sensing and for decorative purposes. Examples of these may be found in D G McDonnell in Thermotropic Liquid Crystals, Critical Reports on Applied Chemistry, Vol. 22, edited by G W Gray, 1987 pp 120-44; this reference also contains a general description of thermochromic cholesteric liquid crystals.

Generally, commercial thermochromic applications require the formulation of mixtures which possess low melting points, short pitch lengths and smectic transitions just below the required temperature-sensing region. Preferably the mixture or material should retain a low melting point and high smectic - cholesteric transition temperatures.

In general, thermochromic liquid crystal devices have a thin film of cholesterogen sandwiched between a transparent supporting substrate and a black absorbing layer. One of the fabrication methods involves producing an 'ink' with the liquid crystal by encapsulating it in a polymer and using printing technologies to apply it to the supporting substrate. Methods of manufacturing the inks include gelatin microencapsulation, US patent 3,585,318 and polymer dispersion, US patents 1,161,039 and 3,872,050. One of the ways for preparing well-aligned thin film structures of cholesteric liquid crystals involves

laminating the liquid crystal between two embossed plastic sheets. This technique is described in UK patent 2,143,323.

Other compounds of the present invention or mixtures of these may be used in ferroelectric mixtures and devices. In particular compounds of the invention may be used in many of the known forms of liquid crystal display devices, for example chiral smectic electro-optic devices. Such a device may comprise a layer of liquid crystal material contained between two spaced cell walls bearing electrode structures and surface treated to align liquid crystal material molecules. Ferroelectric smectic liquid crystal materials, which can be produced by mixing an achiral host and a chiral dopant, use the ferroelectric properties of the tilted chiral smectic C, F, G, H, I, J and K phases. The chiral smectic C phase is denoted S_C* with the asterisk denoting chirality. The S_C phase is generally considered to be the most useful as it is the least viscous. Ferroelectric smectic liquid crystal materials should ideally possess the following characteristics: low viscosity, controllable spontaneous polarisation (Ps) and an S_C phase that persists over a broad temperature range which should include ambient temperature and exhibits chemical and photochemical stability. Materials which possess these characteristics offer the prospect of very fast switching liquid crystal containing devices. Some applications of ferroelectric liquid crystals are described by J S Patel and J W Goodby in Opt. Eng., 1987, 26, 273.

In ferroelectric liquid crystal devices the molecules switch between different alignment directions depending on the polarity of an applied electric field. These devices can be arranged to exhibit bistability where the molecules tend to remain in one of two states until switched to the other switched state. Such devices are termed surface stabilised ferroelectric devices, e.g. as described in US 5061047 and US 4367924 and US 4563059.

This bistability allows the multiplex addressing of quite large and complex devices.

One common multiplex display has display elements, i.e. pixels, arranged in an X, Y matrix format for the display of for example alpha numeric characters. The matrix format is provided by forming the electrodes on one side as a series of column electrodes, and the electrodes on the other slide as a series of row electrodes. The intersections between each column and row form addressable elements or pixels. Other matrix layouts are known, e.g. seven bar numeric displays.

There are many different multiplex addressing schemes. A common feature involves the application of a voltage, called a strobe voltage to each row or line in sequence. Coincidentally with the strobe applied at each row, appropriate voltages, called data voltages, are applied to all column electrodes. The differences between the different schemes lies in the shape of the strobe and data voltage waveforms.

Other addressing schemes are described in GB-2,146, 473-A; GB-2,173,336-A; GB-2,173, 337-A; GB-2, 173629-A; WO 89/05025; Harada et al 1985 S.I.D. Paper 8.4 pp 131-134; Lagerwall et al 1985 I.D.R.C. pp 213-221 and P Maltese et al in Proc 1988 I.D.R.C. pp 90-101 Fast Addressing for Ferroelectric LC Display Panels.

The material may be switched between its two states by two strobe pulses of opposite sign, in conjunction with a data waveform. Alternatively, a blanking pulse may be used to switch the material into one of its states. Periodically the sign of the blanking and the strobe pulses may be alternated to maintain a net d.c. value.

These blanking pulses are normally greater in amplitude and length of application than the strobe pulses so that the

material switches irrespective of which of the two data waveforms is applied to any one intersection. Blanking pulses may be applied on a line by line basis ahead of the strobe, or the whole display may be blanked at one time, or a group of lines may be simultaneously blanked.

It is well known in the field of ferroelectric liquid crystal device technology that in order to achieve the highest performance from devices, it is important to use mixtures of compounds which give materials possessing the most suitable ferroelectric smectic characteristics for particular types of devices.

Devices can be assessed for speed by consideration of the response time vs pulse voltage curve. This relationship may show a minimum in the switching time (t_{min}) at a particular applied voltage (V_{min}). At voltages higher or lower than V_{min} the switching time is longer than t_{min}. It is well understood that devices having such a minimum in their response time vs voltage curve can be multiplex driven at high duty ratio with higher contrast than other ferroelectric liquid crystal devices. It is preferred that the said minimum in the response time vs voltage curve should occur at low applied voltage and at short pulse length respectively to allow the device to be driven using a low voltage source and fast frame address refresh rate.

Typical known materials (where materials are a mixture of compounds having suitable liquid crystal characteristics) which do not allow such a minimum when included in a ferroelectric device include the commercially available materials known as SCE13 and ZLI-3654 (both supplied by Merck UK Ltd, Poole, Dorset). A device which does show such a minimum may be constructed according to PCT GB 88/01004 and utilising materials such as e.g. commercially available SCE8 (Merck UK Ltd). Other examples of prior art materials are exemplified by PCT/GB 86/00040, PCT GB 87/00441 and UK 2232416B.

Certain compounds of the invention may be useful in laser addressed applications in which laser beams are used to scan across the surface of the material or leave a written impression thereon. For various reasons many of these materials have consisted of organic materials which are at least partially transparent in the visible region. The technique relies upon localised absorption of laser energy which causes localised heating and in turn alters the optical properties of the otherwise transparent material in the region of contact with the laser beam. Thus as the beam traverses the material, a written impression of its path is left behind. One of the most important of these applications is in laser addressed optical storage devices, and in laser addressed projection displays in which light is directed through a cell containing the material and is projected onto a screen. Such devices have been described by Khan Appl. Phys. Lett. vol. 22, p111, 1973; and by Harold and Steele in Proceedings of Euro display 84, pages 29-31, September 1984, Paris, France, in which the material in the device was a smectic liquid crystal material. Devices which use a liquid crystal material as the optical storage medium are an important class of such devices. The use of semiconductor lasers, especially Ga_xAl_{1-x} As lasers where x is from 0 to 1, and is preferably 1, has proven popular in the above applications because they can provide laser energy at a range of wavelengths in the near infra-red which cannot be seen and thus cannot interfere with the visual display, and yet can provide a useful source of well-defined, intense heat energy. Gallium arsenide lasers provide laser light at wavelengths of about 850nm, and are useful for the above applications. With increasing Al content ($x< 1$), the laser wavelength may be reduced down to about 750nm. The storage density can be increased by using a laser of shorter wavelength.

Thus some compounds of the present invention may be suitable as optical storage media and may be combined with dyes for use in

laser addressed systems, for example in optical recording media.

The compounds of the present invention may also be used in pyroelectric devices for example detectors, steering arrays and vidicon cameras.

A pyroelectric detector consists of electrode plates at least one of which may be pixellated. In operation the detector is exposed to radiation R, for example infrared radiation, which is absorbed by an electrode. This results in a rise in temperature which is transmitted to a layer of pyroelectric material by conduction, The change in temperature results in a thermal expansion and a charge is generated. This change in charge is usually small when compared with the charge output due to the change in the spontaneous polarisation, Ps with a change in temperature; this constitutes the primary pyroelectric effect. A change in charge results in a change in potential difference between the electrodes. The charge on each pixel may be read out and the resulting signal is used to modulate scanning circuits in, for example, a video monitor and for a visual image of the infra red scans.

The selective reflective properties of the materials described by the current invention may also allow for materials of the current invention to be used in inks and paints and they may therefore be useful in anti-counterfeiting operation. They may also be used in so-called security inks. Other applications include thermal control management, for example the materials may be included in a coating which may be applied to one or more windows in order to reflect infra-red radiation.

Spatial light modulators comprises a liquid crystal cell formed by typically two glass walls and 0.1-10μm e.g. 2.5μm thick spacer. The inner faces of the walls carry thin transparent indium tin oxide electrodes connected to a variable voltage

source. On top of the electrodes are surface alignment layers e.g. of rubbed polyimide described in detail later. Other alignment techniques are also suitable e.g. non-rubbing techniques such as evaporation of SiO_2. A layer of liquid crystal material is contained between the walls and spacer. In front of the cell is a linear polariser; behind the cell is a quarter waveplate (this may be optional) and a mirror. An example of a linear polariser is a polarising beam splitter (not illustrated here).

Suitable devices in which the materials of the current invention may be incorporated include beam steerers, shutters, modulators and pyroelectric and piezoelectric sensors.

The materials of the present invention may also be useful as dopants in ferroelectric liquid crystal devices, which may be multiplexed, or they may be used in active backplane ferroelectric liquid crystal systems. The materials of the present invention may also be useful as host materials. The materials of the present invention may be included in mixtures which also contain one or more dopants.

The invention will now be particularly described by way of example.

Example 1

Preparation of Compound 3 in Table 1

Step 1

Preparation of 1-Bromo-4-heptylbenzene

Anhydrous aluminium chloride (19.8 g, 148 mmol) was added to a stirred solution of heptanoyl chloride (24.2 g, 163 mmol) in dry dichloromethane (135 ml). A solution of bromobenzene (21.2 g, 135 mmol) in dry dichloromethane (45 ml) was added, and the mixture was refluxed overnight with exclusion of moisture. The reaction was monitored by glc analysis. The mixture was cooled in an ice/water bath and poly(methylhydrosiloxane) (21.7 g, 360

mmol) was added dropwise with stirring. The mixture was refluxed overnight, glc analysis indicating complete conversion of the ketone. After removal of the solvent *in vacuo* the residue was poured into an ice/water mixture and sodium hydroxide solution (10%) was added to facilitate layer separation and to remove residual acid chloride. Ether was added and the separated aqueous layer was washed with ether (2 x 200 ml). The combined organic layers were washed with sodium hydroxide solution (10%), water and brine, and dried ($MgSO_4$). Removal of the solvent *in vacuo* gave a residue which was purified by flash chromatography [silica gel / petroleum fraction (bp 40-60 °C)], followed by distillation *in vacuo*. A colourless oil was obtained.

Yield 15.1 g (44%) bp 117 °C at 0.1 mm Hg

^{1}**H NMR** $CDCl_3/\delta$	7.38 (2H, d), 7.04 (2H, d), 2.54 (2H, t), 1.57 (2H, qui) 1.28 (8H, m), 0.88 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2930, 1490, 1073, 828, 799
MS *m/z*	256,254(M^+), 199, 185, 171(100%), 90

Step 2

Preparation of 4-Heptylbenzeneboronic acid

1-Bromo-4-heptylbenzene from step 1 (20.0 g, 78 mmol) in dry tetrahydrofuran(80 ml) was added in one portion to oven-dried magnesium (2.2 g, 90 mmol) in dry tetrahydrofuran (100 ml) with stirring under nitrogen. A crystal of iodine was added, and the mixture refluxed (2.5 h) and then allowed to return to room temperature. Dry tetrahydrofuran (80 ml) was added and the mixture cooled to -40 °C. Trimethyl borate (16.21 g, 156 mmol) was added dropwise, keeping the temperature below -10 °C. The mixture was allowed to return to room temperature and hydrochloric acid (5M, 36 ml) was added whilst stirring (45 min). The mixture was then poured into water and ether added. The separated aqueous layer was washed twice with ether (2 x 200 ml), and the product was extracted from the combined ethereal phases as the sodium salt by washing with potassium

hydroxide (2M, 40 ml), The basic solution was then washed with ether, and the product released by acidification to pH3 by adding hydrochloric acid (conc.) to the aqueous solution. The product was then extracted with ether (2 x 200 ml), which was washed with water and brine, dried ($MgSO_4$), and the solvent removed *in vacuo*.

A pale-brown solid was obtained.

Yield 15.8 g (92%).

MS *m/z* 220(M^+), 192, 135, 122, 107(100%)

Step 3

Preparation of Ethyl 5-bromobenzo[b]furan-2-carboxylate

A mixture of 5-bromosalicylaldehyde (2.0 g, 10 mmol), diethyl bromomalonate (2.0 g, 8.4 mmol), and potassium carbonate (2.5 g, 18 mmol) was refluxed in butanone (30 ml) (7 h). Glc analysis revealed no further reaction. When cool, the solvent was removed *in vacuo*, and water and dichloromethane added. The separated aqueous layer was washed twice with dichloromethane (2 x 100 ml) and the combined organic layers dried ($MgSO_4$). After removal of the solvent *in vacuo* the residue was recrystallised (ethanol).

Pale yellow needle-like crystals were obtained.

Yield 0.9 g (40%), mp 58-60 °C.

^{1}**H NMR** $CDCl_3/\delta$ 7.82 (1H, d), 7.54 (1H, dd), 7.47 (1H, d), 7.46 (1H, s), 4.46 (2H, q), 1.43 (3H, t)

IR (KBr) ν_{max}/cm^{-1} 1730, 1555, 1310, 1185, 855

MS *m/z* 268,270(M^+), 240, 225(100%), 196, 169

Step 4

Preparation of Ethyl 5-(4-heptylphenyl)benzo[b]furan-2-carboxylate

Ethyl 5-bromobenzo[b]furan-2-carboxylate (2.0 g, 7.4 mmol) from step 3, sodium carbonate (2.0 g, 18.5 mmol), 1,2-dimethoxyethane (10 ml) and water (30 ml), were stirred under nitrogen. Tetrakis(triphenylphosphine)palladium(0) (0.3 g, 0.3

mmol) was added, followed by 4-heptylbenzeneboronic acid from step 2 (2.0 g, 8.9 mmol) in 1,2-dimethoxyethane (20 ml), and the mixture refluxed (4 h). Completion of the reaction was indicated by glc and tlc analysis. After allowing to cool, the reaction mixture was poured into water and ether added. The separated aqueous layer was washed with ether (2 x 100 ml), and the combined ethereal layers washed with water and brine and dried ($MgSO_4$). After removal of the solvent *in vacuo* the residue was purified by flash chromatography [silica gel / petroleum fraction (bp 40-60 °C) (impurity); petroleum fraction (bp 40-60 °C), dichloromethane 7:3 (product)]. The product was recrystallised (hexane).

Colourless needles were obtained.

Yield 1.3 g (48%), mp 46-8 °C.

^{1}H NMR $CDCl_3/\delta$	7.84 (1H, dd), 7.67 (1H, dd), 7.63 (1H, d), 7.56 (1H, d), 7.52 (2H, d), 7.27 (2H, d), 4.46 (2H, q), 2.65 (2H, t), 1.65 (2H, qui), 1.44 (3H, t), 1.33 (8H, m), 0.89 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2930, 1725, 1560, 1160, 1095
MS *m/z*	364(M^+)(100%), 279, 264, 251, 220

Step 5

Preparation of 5-(4-Heptylphenyl)benzo[b]furan-2-carboxylic acid

Potassium hydroxide (0.5 g, 6.8 mmol) in ethanol (30 ml) and water (3 ml) was added to ethyl 5-(4-heptylphenyl)benzo{b} furan-2-carboxylate from step 4 (1.2 g, 3.4 mmol).and the mixture was refluxed (5 min) with stirring. The solvent was then removed *in vacuo* and water added to the residue, which was then adjusted to pH 3 by adding hydrochloric acid (2M). The precipitated white solid was then filtered off and dried *in vacuo* ($CaCl_2$), and recrystallised (acetic acid).

White, fibrous needles were obtained.

Yield 0.7 g (63%).

Transitions (°C) K 131 SmC 185 N 222 Iso.

^{1}**H NMR** $CDCl_3/\delta$	7.88 (1H, dd), 7.74 (1H, dd), 7.74 (1H, d), 7.67 (1H, d), 7.54 (2H, d), 7.28 (2H, d), 7.27 (1H, s), 2.66 (2H, t), 1.65 (2H, qui), 1.33 (8H, m), 0.89 (3H, m)
IR (KBr) ν_{max}/cm^{-1}	2950, 2850, 1690, 1575, 1310, 1170, 805
MS *m/z*	336(M^+), 292, 251(100%), 231, 207

Step 6

Preparation of 5-(4-heptylphenyl)benzo[b]furan-2-carboxamide

A mixture of 5-(4-heptylphenyl)benzo[b]furan-2-carboxylic acid from step 5 (0.70 g, 2.1 mmol) and thionyl chloride (0.75 g, 6.3 mmol) in dry benzene (25 ml) was refluxed (4 h) with exclusion of moisture. The solvent was then removed *in vacuo*, and the crude acid chloride dissolved in dry tetrahydrofuran (20 ml). Ammonia (d 0.880, 0.7 ml) was then added with stirring. After stirring for a further 30 min, water (40 ml) was added and the precipitate filtered off and washed with cold water. It was then recrystallised (ethanol), and dried *in vacuo* overnight ($CaCl_2$).

White crystals were obtained.

Yield 0.55 g (78%), mp 201-2 °C.

^{1}**H NMR** $CDCl_3/\delta$	7.86 (1H, dd), 7.66 (1H, dd), 7.56 (1H, d), 7.56 (1H, d) 7.53 (2h, d), 7.27 (2H, d), 6.54 (1H, s), 5.65 (1H, s) 2.66 (2H, t), 1.66 (2H, qui), 1.31 (8H, m), 0.89 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	3471, 3396, 3183, 2922, 2849, 1661, 1616, 1395, 801
MS *m/z*	335(M^+), 250(100%), 191, 178, 165

Step 7

Preparation of 2-Cyano-5-(4-heptylphenyl)benzo[b]furan (Compound 3)

Thionyl chloride (1.8 g, 15 mmol) was added to a stirred solution of 5-(4-heptylphenyl)benzo[b]furan-2-carboxamide (0.5 g, 1.5 mmol) from step 6 in dry *N,N*-dimethylformamide (10 ml)

under nitrogen. The mixture was stirred overnight, and then poured into an ice/water mixture. The product was extracted with ether (2 x 100 ml), and the combined extractions were washed with water and saturated sodium bicarbonate solution and dried ($MgSO_4$). The solvent was removed *in vacuo* and the product purified by flash chromatography [silica gel / petroleum fraction (bp 40-60 °C), dichloromethane 1:1], followed by recrystallization (ethanol).

Colourless crystals were obtained.

Yield 0.3 g (63%). Purity (hplc) >99%.

Transitions (°C) K 31.1 N 60.5 Iso.

^{1}**H NMR** $CDCl_3/\delta$	7.83 (1H, d), 7.73 (1H, dd), 7.60 (1H, d), 7.51 (2H, d), 7.50 (1H, s), 7.28 (2H, d), 2.66 (2H, t), 1.65 (2H, qui), 1.33 (8H, m), 0.89 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2920, 2850, 2230, 1460, 1130, 885, 800
MS *m/z*	317(M^+), 232(100%), 203, 190, 176

Example 2

Preparation of Compound No. 25 in Table 1

Step 1

Preparation of 5-Bromobenzo[b]furan-2-carboxylic acid

The title compound was prepared and purified in a similar manner to that described in Example 1 step 5 but using as starting material, ethyl 5-bromobenzo{b}furan-2-carboxylate (prepared as described in Example 1 step 3) (27.5 g, 102 mmol), potassium hydroxide (11.5 g, 204 mmol).

White crystals were obtained.

Yield 16.6 g (68%), mp >290 °C.

^{1}**H NMR** CD_2Cl_2/δ	7.80 (1H, dd), 7.49 (1H, dd), 7.44 (1H, d), 7.38 (1H, d)
IR (KBr) ν_{max}/cm^{-1}	3417, 1738, 1556, 1395, 1051, 946, 873, 803, 779
MS *m/z*	241(M^+), 223, 169, 89, 62(100%)

Step 2

Preparation of 5-Bromobenzo[b]furan-2-carboxamide

5-Bromobenzo[b]furan-2-carboxylic acid from step 1 (16.5 g, 69 mmol), thionyl chloride (24.4 g, 205 mmol), ammonia (d 0.880, 46 ml) was converted to 5-bromobenzo[b]furan-2-carboxamide using a method analogous to that described in Example 1 step 6. White needles were obtained.

Yield 9.9 g (60%), mp 212-215 °C.

^{1}**H NMR** DMSO-d^6/δ	7.80 (1H, d), 7.51 (1H, d), 7.40 (1H, dd), 7.32 (2H, s), 6.95 (1H, d)
IR (KBr) ν_{max}/cm^{-1}	3024, 2860, 1591, 1563, 1473, 1318, 1179, 789, 422
MS *m/z*	240(M$^+$), 223, 169, 89, 62(100%)

Step 3

Preparation of 2-Cyano-5-bromobenzo[b]furan

5-Bromobenzo[b]furan-2-carboxamide (9.8 g, 41 mmol) prepared as described in step 2, thionyl chloride (49.2 g, 410 mmol) were reacted using a method analogous to that described above in Example 1 step 7 to yield 2-Cyano-5-bromobenzo[b]furan. Off-white needles were obtained.

Yield 4.6 g (51%), mp 152.5-153.5 °C.

^{1}**H NMR** CD_2Cl_2/δ	7.86 (1H, dd), 7.63 (1H, dd), 7.47 (1H, dd), 7.46 (1H, d)
IR (KBr) ν_{max}/cm^{-1}	2230, 1552, 1437, 1183, 949, 810, 571, 478
MS *m/z*	223,221(M$^+$)(100%), 142, 114, 87, 58

Step 4

Preparation of 1-Bromo-4-propylbenzene

Bromobenzene (31.4 g, 200 mmol), propionyl chloride (22.2 g, 240 mmol), aluminium chloride (29.5 g, 220 mmol), poly(methylhydrosiloxane) (32.1 g 533 mmol) were converted to 1-bromo-4-propylbenzene using a method analogous to that described in Example 1 step 1 .

A colourless liquid was obtained.

Yield 19.2 g (48%), bp 115 °C at 0.03 mm Hg.

^{1}H **NMR** $CDCl_3/\delta$	7.38 (2H, d), 7.05 (2H, d), 2.51 (2H, t), 1.61 (2H, sxt), 0.92 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2965, 2871, 1489, 1077, 1011, 828, 796
MS *m/z*	200,198(M^+), 169(100%), 119, 103, 90

Step 5

Preparation of 4-Propylbenzeneboronic acid

1-Bromo-4-propylbenzene (11.0 g, 55 mmol) obtained in step 2, magnesium (1.5 g, 61 mmol), trimethyl borate (11.4 g, 110 mmol) were reacted using a method analogous to that described in Example 1 step 2. An off-white solid was obtained.

Yield 7.5 g (83%).

MS *m/z*	164(M^+), 147, 135, 91, 43(100%)

Step 6

Preparation of 2-Cyano-5-(4-propylphenyl)benzo[b]furan (Compound 25 in Table 1)

2-Cyano-5-bromobenzo{b}furan obtained as described in step 3 above (1.0 g, 4.5 mmol), 4-propylbenzene boronic acid obtained as described in step 5 above (0.9 g, 5.4 mmol), sodium carbonate (1.2 g, 11.3 mmol), tetrakis(triphenylphosphine)palladium(0) (0.3 g, 0.3 mmol) were reacted using a method analogous to that described in Example 1 step 4 to yield compound 25 in table 1 as white crystals.

Yield 0.3 g (26%). Purity (hplc) >99%.

Transitions (°C) K 58.0 (48.9 N) Iso.

^{1}H **NMR** CD_2Cl_2/δ	7.86 (1H, dd), 7.75 (1H, dd), 7.62 (1H, d), 7.55 (1H, d), 7.52 (2H, d), 7.29 (2H, d), 2.64 (2H, t), 1.67 (2H, sxt), 0.97 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2962, 2871, 2229, 1560, 1460, 1266, 1126, 885, 801, 612
MS *m/z*	261(M^+), 232(100%), 203, 176, 151

Example 3

Preparation of Compound 26 in Table 1

Step 1

Preparation of 1-Bromo-4-pentylbenzene

Bromobenzene (21.2 g, 135 mmol), valeryl chloride (19.7 g, 163 mmol), aluminium chloride (19.8 g, 148 mmol), poly(methylhydrosiloxane) (21.7 g, 360 mmol) were reacted using a method analogous to that described in Example 1 step 1 to yield 1-bromo-4-pentylbenzene as a colourless liquid .

Yield 11.6 g (38%) bp 100 °C at 0.2 mm Hg.

^{1}H NMR $CDCl_3/\delta$	7.38 (2H, d), 7.04 (2H, d), 2.54 (2H, t), 1.58 (2H, qui), 1.31 (4H, m), 0.88 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2929, 2858, 1486, 1073, 830, 796
MS *m/z*	228,226(M^+), 198, 183, 171(100%), 157

Step 2

Preparation of 4-Pentylbenzeneboronic acid

Using a method analogous to that described in Example 1 step 2, the title compound was obtained from 1-bromo-4-penyltbenzene from Step 1 (15.2 g, 67 mmol), magnesium (1.9 g, 77 mmol), and trimethyl borate (13.9 g, 134 mmol). The product was obtained as a waxy white solid.

Yield 6.4 g (50%).

MS *m/z* 522($3M^+$-$3H_2O$), 465(100%), 409, 352, 175

Step 3

Preparation of 2-Cyano-5-(4-pentylphenyl)benzo[b]furan (Compound 26 in Table 1)

2-Cyano-5-bromobenzo[b}furan obtained as described in Example 2 step 3 (0.6 g, 2.7 mmol), 4-pentylbenzeneboronic acid from step 2 above (0.6 g, 3.2 mmol), sodium carbonate (0.7 g, 6.8 mmol), tetrakis(triphenylphosphine)palladium(0) (0.2 g, 0.1 mmol) were reacted together in a method analogous to that described in Example 1 step 4 to give the desired compound as colourless plates.

Yield 0.3 g (38%). Purity (hplc) >99%.
Transitions (°C) K 51.1 N 56.4 Iso.

^{1}**H NMR** CD_2Cl_2/δ	7.87 (1H, dd), 7.75 (1H, dd), 7.61 (1H, ddd), 7.54 (1H, d), 7.52 (2H, d), 7.28 (2H, d), 2.66 (2H, t), 1.65 (2H, qui), 1.34 (4H, m), 0.91 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2965, 2861, 2232, 1558, 1439, 1187, 949, 819, 524
MS *m/z*	289(M^+), 232(100%), 203, 189, 176

Example 4

Preparation of Compound 40 in Table 1

Step 1

Preparation of 1-Bromo-4-hexylbenzene

1-Bromo-4-hexylbenzene was prepared and purified using a method analogous to that described in Example 1 step 1 but using as starting materials, bromobenzene (21.2 g, 135 mmol), hexanoyl chloride (20.0 g, 149 mmol), aluminium chloride (19.9 g, 149 mmol), and poly(methylhydrosiloxane) (21.7 g, 360 mmol). A colourless liquid was obtained.

Yield 10.4 g (32%), bp 110 °C at 0.01 mm Hg.

^{1}**H NMR** $CDCl_3/\delta$	7.38 (2H, d), 7.03 (2H, d), 2.54 (2H, t), 1.57 (2H, qui), 1.29 (6H, m), 0.88 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2933, 2861, 1489, 1075, 807, 525
MS *m/z*	242,240(M^+), 171(100%), 103, 91

Step 2

Preparation of 4-Hexylbenzeneboronic acid

4-Hexylbenzeneboronic acid was obtained from the product of step 1(8.0 g, 33 mmol), magnesium (1.0 g, 40 mmol), and trimethyl borate (6.9 g, 66 mmol) using a method analogous to that describedin Example1 step 2.
A light-brown solid was obtained.

Yield 4.8 g (71%).

MS *m/z*	564($3M^+$-$3H_2O$), 535, 507, 493, 117(100%)

Step 3

Preparation of 2-Cyano-5-(4-hexylphenyl)benzo[b]furan (Compound 40 in Table 1)

2-Cyano-5-bromobenzo[b]furan obtained as described in Example 2 step 3 (1.0 g, 4.5 mmol), 4-hexylbenzeneboronic acid (obtained as described in step 2 above) (1.0 g, 5 mmol), sodium carbonate (1.2 g, 11 mmol) and tetrakis(triphenylphosphine)palladium(0) (0.3 g, 0.3 mmol) were reacted together in a method analogous to that described in Example 1 step 4. Compound 40 in Table 1 was obtained as colourless crystals.

Yield 0.3 g (22%).

Purity (hplc) 99%.

Transitions (°C) K 25.4 N 45.2 Iso.

^{1}**H NMR** $CDCl_3/\delta$	7.83 (1H, d), 7.73 (1H, dd), 7.60 (1H, d), 7.51 (2H, d), 7.49 (1H, s), 7.28 (2H, d), 2.66 (2H, t), 1.66 (2H, qui), 1.39-1.31 (6H, m), 0.90 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2933, 2861, 2235, 1561, 1271, 1128, 951, 808
MS *m/z*	303(M^+), 274, 246, 232(100%), 219

Example 5

Preparation of Compound 36 in Table 1

Step 1

Preparation of 1-Bromo-4-octylbenzene

The title was prepared and purified using a method analogous to that described in Example 1 step 1 but using the following starting materials:

Bromobenzene (21.2 g, 135 mmol), nonanoyl chloride (24.2 g, 149 mmol), aluminium chloride (19.9 g, 149 mmol), poly(methylhydrosiloxane) (21.7 g, 360 mmol).

A colourless liquid was obtained.

Yield 16.4 g (45%), bp 158 °C at 0.9 mm Hg.

^{1}**H NMR** CD_2Cl_2/δ	7.37 (2H, d), 7.06 (2H, d), 2.54 (2H, t),

	1.56 (2H, qui), 1.26 (10H, m), 0.86 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2932, 2859, 1489, 1074, 803, 519
MS *m/z*	270,268(M^+), 211, 169(100%), 155, 89

Step 2

Preparation of 4-Octylbenzeneboronic acid

4-Octylbenzeneboronic acid was prepared and purified using a method analogous to that described in Example 1 step 2 using the following materials:

1-Bromo-4-octylbenzene from step 1(6.0 g, 22 mmol), magnesium (0.7 g, 27 mmol), trimethyl borate (4.6 g, 44 mmol).

A pale-yellow solid was obtained.

Yield 4.2 g (82%).

MS *m/z*	648($3M^+-3H_2O$), (100%), 551, 452, 353, 187

Step 3

Preparation of 2-Cyano-5-(4-octylphenyl)benzo[b]furan (Compound 36 in Table 1)

Compound 36 was prepared and purified in a similar manner to that described in Example 1 step 4 from the following materials:

4-octylbenzeneboronic acid from step 2 (2.0 g, 8.5 mmol), 2-cyano-5-bromobenzo[b]furan (obtained as described in Example 2 step 3)(1.6 g, 7.1 mmol), sodium carbonate (1.9 g, 18 mmol), tetrakis(triphenylphosphine)palladium(0) (0.2 g, 0.2 mmol)

A colourless liquid crystal was obtained.

Yield 0.5 g (21%).

Purity (hplc) 98.5%.

Transitions (°C) K 28.2 SmA 34.3 N 48.8 Iso.

^{1}H NMR CD_2Cl_2/δ	7.87 (1H, dd), 7.45 (1H, dd), 7.62 (1H, d), 7.55 (1H, d), 7.53 (2H, d), 7.29 (2H, d), 2.66 (2H, t), 1.65 (2H, qui), 1.35-1.29 (10H, m), 0.89 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2932, 2859, 2235, 1561, 1464, 1184, 951, 807
MS *m/z*	331(M^+), 260, 232(100%), 203, 57

Example 6

Preparation of Compound 34 in Table 1

Step 1

Preparation of 1-Bromo-4-nonylbenzene

The title compound was prepared and purified in a similar manner to that described in Example 1 step 1 from the following reagents:

Bromobenzene (21.2 g, 135 mmol), nonanoyl chloride (26.3 g, 149 mmol), aluminium chloride (19.9 g, 149 mmol), poly(methylhydrosiloxane) (21.7 g, 360 mmol).

A colourless liquid was obtained, which solidified to a waxy solid on standing.

Yield 7.0 g (18%), bp 145 °C at 0.01 mm Hg.

^{1}H NMR $CDCl_3/\delta$	7.38 (2H, d), 7.04 (2H, d), 2.54 (2H, t), 1.58 (2H, qui), 1.27 (12H, m), 0.88 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2934, 2859, 1490, 1074, 825, 798, 634, 510
MS *m/z*	284,282(M^+), 169, 91(100%), 71

Step 2

Preparation of 4-Nonylbenzeneboronic acid

The title compound was prepared and purified in a similar manner to that described in Example 1 step using the following reagents:

1-Bromo-4-nonylbenzene from step 1(5.0 g, 18 mmol), magnesium (0.5 g, 22 mmol), trimethyl borate (3.7 g, 36 mmol).

A waxy white solid was obtained.

Yield 3.7 g (83%).

MS *m/z*	691($3M^+-3H_2O$), 578, 452, 354, 117(100%)

Step 3

Preparation of 2-Cyano-5-(4-nonylphenyl)benzo[b]furan (Compound 34 in Table 1)

Compound 34 was prepared and purified in a similar manner to that described in Example 1 step 4 from the following reagents:

4-nonylbenzeneboronic acid from step 2 (1.2 g, 5 mmol), 2-cyano-5-bromobenzo[b]furan (obtained as described in Example 2 step 3) (1.0 g, 4.5 mmol), sodium carbonate (1.2 g, 11 mmol), tetrakis(triphenylphosphine)palladium(0) (0.3 g, 0.3 mmol) Colourless needles were obtained.

Yield 0.5 g (32%).

Purity (hplc) 98.6%.

Transitions (°C) K 28.1 SmA 49.6 N 60.0 Iso.

^{1}H NMR CD_2Cl_2/δ	7.86 (1H, dd), 7.75 (1H, dd), 7.61 (1H, d), 7.55 (1H, d), 7.52 (2H, d), 7.29 (2H, d), 2.66 (2H, t), 1.65 (2H, qui), 1.31 (12H, m), 0.89 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2929, 2858, 2333, 1464, 1127, 950, 887, 805
MS *m/z*	345(M^+), 231(100%) 218, 190, 176

Example 7

Preparation of Compound 16 in Table 1

Step 1

Preparation of 4-Nonyloxybenzeneboronic acid

The title compound was prepared and purified in a similar manner to that described in Example 1 step 2 using the following reagents:

4-Nonyloxybromobenzene (5.0 g, 17 mmol), magnesium (0.5 g, 22 mmol), trimethyl borate (3.5 g, 34 mmol).

A pale yellow solid was obtained.

Yield 4.0 g (88%).

MS *m/z*	264(M^+), 238, 220, 151, 94(100%)

Step 2

Preparation of Ethyl 5-(4′-nonyloxyphenyl)benzo[b]furan-2-carboxylate

Ethyl 5-bromobenzo[b]furan-2-carboxylate (obtained as described in Example 1 step 3) (1.5 g, 14 mmol), 4-nonyloxybenzeneboronic acid (1.8 g, 7 mmol), sodium carbonate (1.5 g, 14 mmol), tetrakis(triphenylphosphine)palladium(0) (0.2 g, 0.2 mmol) were reacted together using a method analogous to that described in

Example 1 step 4. Ethyl 5-(4′-nonyloxyphenyl)benzo[b]furan-2-carboxylate was obtained as a white solid.

Yield 0.7 g (31%).

Transitions (°C) K 85.8 (84.6 SmA) Iso.

^{1}H NMR CD_2Cl_2/δ	7.83 (1H, d), 7.66 (1H, dd), 7.62 (1H, d), 7.55 (1H, s), 7.54 (2H, d), 6.98 (2H, d), 4.41 (2H, q), 4.00 (2H, t), 1.80 (2H, qui), 1.41 (2H, t), 1.30 (12H, m), 0.89 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2923, 2852, 1722, 1607, 1574, 1517, 1164, 945, 839, 747
MS *m/z*	408(M^+), 281, 227, 97, 57(100%)

Step 3

Preparation of 5-(4-Nonyloxyphenyl)benzo[b]furan-2-carboxylic acid

5-(4-Nonyloxyphenyl)benzo[b]furan-2-carboxylic acid was prepared and purified in a similar manner to that described in Example 1 step 5 using the following reagents:

Ethyl 5-(4′-nonyloxyphenyl)benzo[b]furan-2-carboxylate from step 2(0.7 g, 1.7 mmol), potassium hydroxide (0.2 g, 3.4 mmol). A white crystalline solid was obtained.

Yield 0.5 g (77%).

Transitions (°C) K 212.2 SmC 223.0 Iso.

^{1}H NMR CD_2Cl_2/δ	7.87 (1H, d), 7.72 (1H, dd), 7.69 (1H, s), 7.65 (1H, d), 7.54 (2H, d), 6.99 (2H, d), 4.01 (2H, t), 1.80 (2H, qui), 1.48 (2H, m), 1.30 (10H, m), 0.89 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	3420, 2920, 2840, 2547, 1690, 1515, 1174, 942, 748
MS *m/z*	380(M^+), 254(100%) 225, 210, 180

Step 4

Preparation of 5-(4-Nonyloxyphenyl)benzo[b]furan-2-carboxamide

The product of step 3 (0.9 g, 2.4 mmol), thionyl chloride (0.9 g, 7.2 mmol), and ammonia (d 0.880, 1.4 ml) were used in a method analogous to that described in Example 1 step 6 to yield the desired compound as a white crystalline solid.

Yield 0.8 g (82%), mp 201-202 °C.

^{1}**H NMR** CD_2Cl_2/δ	7.83 (1H, dd), 7.65 (1H, dd), 7.57 (1H, d), 7.54 (2H, d), 7.49 (1H, d), 6.99 (2H, d), 6.53 (1H, s), 5.65 (1H, s), 4.00 (2H, t), 1.80 (2H, qui), 1.41 (12H, m), 0.88 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	3462, 2919, 2851, 1678, 1601, 1518, 1166, 941, 812
MS *m/z*	379(M^+), 253(100%) 225, 181, 152

Step 5

Preparation of 2-Cyano-5-(4-nonyloxyphenyl)benzo[b]furan (Compound 16 in Table 1)

Compound 16 was prepared and purified in a similar manner to that described in Example 1 step 7 using the quantities stated. The product of step 4 (0.7 g, 1.9 mmol), thionyl chloride (2.3 g, 19 mmol).

Colourless plate-like crystals were obtained.

Yield 0.1 g (15%).

Purity (hplc) 99.9%.

Transitions (°C) K 62 SmA 87 N 97 Iso

^{1}**H NMR** CD_2Cl_2/δ	7.80 (1H, d), 7.70 (1H, dd), 1.58 (1H, d), 7.52 (1H, s), 7.51 (2H, d), 6.97 (2H, d), 3.98 (2H, t), 1.78 (2H, qui), 1.46 (2H, m0, 1.28 (10H, m), 0.87 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2930, 2859, 2236, 1688, 1517, 1182, 1032, 842, 808
MS *m/z*	361(M^+), 248, 235(100%), 206

Example 8

Preparation of Compound 41 in Table 1

Step 1

Preparation of 2-(4-Pentylcyclohexyl)phenoxy)acetaldehyde dimethyl acetal

A mixture of 4-(4-pentylcyclohexyl)phenol (10.0 g, 41 mmol), bromoacetaldehyde dimethyl acetal (10.1 g, 60 mmol), potassium carbonate (11.1 g, 80 mmol) and potassium iodide (0.5 g, 3 mmol) in cyclopentanone (60 ml) was refluxed under nitrogen with stirring (48 h). The reaction was monitored by glc analysis. After allowing to cool, the mixture was poured into water and ether added. The separated aqueous phase was saturated with salt and washed with ether 2 x 200 ml). The combined organic layers were washed with sodium hydroxide solution (10%), water, dried (Na_2SO_4), and the solvent removed *in vacuo*. The crude product was purified by flash chromatography [neutral alumina / petroleum fraction (bp 40-60 °C), dichloromethane 1:1].

A pale yellow liquid was obtained.

Yield 10.1 g (75%), bp 195 °C at 0.01 mm Hg.

^{1}H NMR CD_2Cl_2/δ	7.11 (2H, d), 6.82 (2H, d), 4.66 (1H, t), 3.94 (2H, d), 3.41 (6H, s), 2.83-2.80 (1H, m), 1.73-1.66 (4H, m), 1.45-1.38 (1H, m), 1.35-1.20 (10H, m), 1.08-1.02 (2H, m), 0.89 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2928, 2860, 1709, 1644, 1514, 1139, 1081, 828
MS *m/z*	334(M^+), 260, 176, 133, 75(100%)

Step 2

Preparation of 5-(4-Pentylcyclohexyl)benzo[b]furan

The product of step 1 (10.1 g, 31 mmol) was added dropwise to polyphosphoric acid (13 g) in chlorobenzene (130 ml) under reflux with stirring. The mixture was refluxed overnight (glc analysis indicated a complete reaction), and allowed to cool.

The solvent was removed *in vacuo* and sodium hydroxide solution (10%) and ether were added. The separated aqueous layer was washed with ether (2 x 200 ml) and the combined organic layers washed with water and brine, and dried ($MgSO_4$). The solvent was removed *in vacuo* and the crude product purified by flash chromatography [silica gel / petroleum fraction (bp 40-60 °C)], followed by distillation.

A pale-yellow liquid was obtained.

Yield 4.1 g (48%), bp 165 °C at 0.01 mm Hg.

^{1}**H NMR** CD_2Cl_2/δ	7.76 (1H, d), 7.34 (1H, d), 7.31 (1H, d), 7.07 (1H, dd), 6.64 (1H, dd), 2.48 (1H, tt), 1.84-1.77 (4H, m), 1.44 (1H, dd), 1.38 (1H, dd), 1.26-1.14 (9H, m), 1.02 (1H, dd), 0.95 (1H, dd), 0.83 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2927, 2856, 1514, 1455, 1197, 877, 809, 735
MS *m/z*	270(M^+), 199, 171, 157(100%), 131

Step 3

Preparation of 5-(4-Pentylcyclohexyl)benzo[b]furan-2-carboxylic acid

A flask containing the product of step 2 (1.7 g, 6.3 mmol) in dry tetrahydrofuran (70 ml) was flushed with nitrogen, degassed, flushed again with nitrogen and cooled (-70 °C). n-Butyllithium (2.5M in hexanes, 2.7 ml, 6.7 mmol) was then added dropwise with stirring, which was continued (0.5 h) at -70 °C. The mixture was then poured into a stirred slurry of 'Cardice' in dry tetrahydrofuran, and allowed to return to room temperature with continuous stirring. The solvent was removed *in vacuo*. The residue was dissolved in glacial acetic acid and the resulting solution was poured into water. The solid was filtered off, washed with water and dried *in vacuo* (KOH).

A white solid was obtained.

Yield 0.2 g (10%).

^{1}**H NMR** CD_2Cl_2/δ	7.47 (1H, d), 7.44(1H, d), 7.39 (1H, s), 7.27 (1H, dd), 2.54 (1H, tt), 1.89-1.83 (4H,

m), 1.49 (1H, dd), 1.42 (1H, dd), 1.31-1.19 (9H, m), 1.07 (1H, dd), 1.10 (1H, dd), 0.86 (3H, t)
(acidic proton signal was not shown)

IR (KBr) ν_{max}/cm^{-1} 3100, 2926, 2853, 1692, 1580, 1425, 943, 828

MS *m/z* 314(M^+), 260, 201, 188(100%), 175

Step 4

Preparation of 5-(4-Pentylcyclohexyl)benzo[b]furan-2-carboxamide

The title compound was prepared and purified in a similar manner to that described in Example 1 step 6 using the following reagents:

The product of step 3 (0.2 g, 0.6 mmol), thionyl chloride (0.2 g, 1.8 mmol), ammonia (d 0.880, 0.4 ml).

Colourless needle-like crystals were obtained.

Yield 0.08 g (50%), mp 214-215 °C

^{1}H NMR CD_2Cl_2/δ 7.51 (1H, d), 7.43 (1H, d), 7.41 (1H, d), 7.31 (1H, dd), 6.51 (1H, s, br), 5.69 (1H, s, br), 2.59 (1H, tt), 1.93-1.88 (4H, m), 1.55-1.45 (2H, m), 1.33-1.21 (9H, m), 1.36-1.03 (2H, m), 0.90 (3H, t)

IR (KBr) ν_{max}/cm^{-1} 3424, 3167, 2926, 2854, 1659, 1613, 1449, 1198, 939, 888

MS *m/z* 313(M^+), 200, 187(100%), 187, 115

Step 5

Preparation of 2-Cyano-5-(4-pentylcyclohexyl)benzo[b]furan (Compound 41 in Table 1)

Compound 41 was prepared and purified in a similar manner to that described in Example 1 step 7 using the following reagents:

5-(4-pentylcyclohexyl)benzo[b]furan-2-carboxamide from step 4(0.05 g, 0.2 mmol), thionyl chloride (0.2 g, 1.4 mmol).

A white solid was obtained.

Yield 0.03 g (60%).

Purity (hplc) >99%.

Transitions (°C) K 77.6 (N 58.5) Iso.

^{1}**H NMR** CD_2Cl_2/δ	7.51 (1H, dd), 7.47 (1H, ddd), 7.45 (1H, d), 7.39 (1H, dd), 2.60 (1H, tt), 1.93-1.87 (4H, m), 1.52-1.43 (2H, m), 1.33-1.21 (9H, m), 1.14-1.03 (2H, m), 0.90 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2924, 2852, 2230, 1557, 1465, 1198, 950, 874, 845, 815
MS *m/z*	295(M^+), 252, 224, 182, 169(100%)

Example 9

Preparation of Compound 42 in Table 1

Step 1

Preparation of 2-(4-Bromophenoxy)acetaldehyde dimethyl acetal

A mixture of 4-bromophenol (87.2 g, 504 mmol), bromoacetaldehyde dimethyl acetal (85.2 g, 520 mmol), potassium carbonate (71.9 g, 520 mmol) and potassium iodide (4.2 g, 25 mmol) in butanone (500 ml) was refluxed under nitrogen with stirring (48 h). The reaction was monitored by glc analysis. After allowing to cool, the mixture was poured into water and ether added. The separated aqueous phase was saturated with salt and washed with ether (3 x 300 ml). The combined organic layers were washed with sodium hydroxide solution (10%), and water, dried (Na_2SO_4), and the solvent removed *in vacuo*. The crude product was then purified by flash chromatography [neutral alumina / dichloromethane], and distillation.

Yield 52.6 g (40%), bp 105 °C at 0.25 mm Hg.

^{1}**H NMR** $CDCl_3/\delta$	7.37 (2H, d), 6.81 (2H, d), 4.70 (1H, t), 3.97 (2H, d), 3.45 (6H, s)
IR (KBr) ν_{max}/cm^{-1}	2940, 1555, 1485, 1070, 820, 645, 505
MS *m/z*	262,260(M^+), 231, 199, 173, 75(100%)

Step 2

Preparation of 5-Bromobenzo[b]furan

5-Bromobenzo[b]furan was prepared and purified in a similar manner to that described in Example 8 step 2 using the following reagents:

The product of step 1 (52.6 g, 202 mmol), polyphosphoric acid (85.0 g).

A colourless liquid was obtained.

Yield 20.2 g (51%), bp 80 °C at 0.01 mm Hg (lit.[2] 15°C).

^{1}H NMR $CDCl_3/\delta$	7.72 (1H, dd), 7.61 (1H, d), 7.38 (1H, dd), 6.71 (1H, d), 7.37 (1H, d)
IR (KBr) ν_{max}/cm^{-1}	1440, 1165, 1030, 800, 760, 670, 420
MS *m/z*	198,196(M^+), 168, 155, 117, 89(100%)

Step 3

Preparation of 5-Cyanobenzo[b]furan

A mixture of the product of step 2 (20.0 g, 102 mmol) and cuprous cyanide monohydrate (22.0 g, 204 mmol) in *N*-methylpyrrolidin-2-one (700 ml) was refluxed (24 h) with stirring. Reaction completion was indicated by glc analysis. The reaction mixture was allowed to cool and filtered through a pad of 'Hyflo Supercel'. It was then poured into water and ether added. The separated aqueous layer was extracted with ether (2 x 300 ml). The combined ethereal layers were washed with water and brine, dried ($MgSO_4$), and the solvent removed *in vacuo*. The desired product was recrystallised from cyclohexane.

Colourless needles were obtained.

Yield 6.6 g (45%), mp 82-83 °C.

^{1}H NMR CD_2Cl_2/δ	7.98 (1H, dd), 7.78 (1H, d), 7.61 (1H, d), 7.60 (1H, dd), 6.89 (1H, dd)
IR (KBr) ν_{max}/cm^{-1}	3150, 2200, 1755, 1600, 1550, 1185, 1010, 885, 760, 610
MS *m/z*	143(M^+), (100%), 88, 62, 50

Step 4

Preparation of 5-Cyanobenzo[b]furan-2-boronic acid

A solution of the product of step 3 (6.5 g, 45 mmol) in dry tetrahydrofuran (150 ml) was degassed and flushed with nitrogen. It was then cooled (-90°C) and n-butyllithium (2.5M in hexanes, 19.1 ml, 48 mmol) was added dropwise with stirring. Stirring was continued (0.5 h), and trimethyl borate (9.4 g, 90 mmol) was added at -100 °C. After stirring (20 min), hydrochloric acid (2M, 137 ml) was added and the mixture stirred for a further 15 min. After allowing to return to room temperature, the mixture was poured into water and ether added. The separated aqueous layer was washed with ether (2 x 200 ml). The combined organic layers were washed with water and brine, dried ($MgSO_4$), and the solvent removed *in vacuo*.

An off-white solid was obtained.

Yield 7.2 g (86%).

MS *m/z* 187(M^+), 160, 145, 117, 43(100%)

Step 5

Preparation of 2-(4-Propylphenyl)-5-cyanobenzo[b]furan (Compound 42 in Table 1)

Compound was prepared and purified in a similar manner to that described in Example 1step 4 using the following reagents: 1-bromo-4-propylbenzene obtained as described in Example 2 step 4 (1.0 g, 5 mmol), the product of step 4 above (1.1 g, 6 mmol), sodium carbonate (1.3 g, 13 mmol), tetrakis(triphenylphosphine)palladium(0) (0.3 g, 0.3 mmol). Colourless crystals were obtained.

Yield 0.1 g (8%).

Purity (hplc) 98%.

Transitions (°C) K 98.0 Iso.

^{1}H NMR CD_2Cl_2/δ 7.93 (1H, dd), 7.79 (2H, d), 7.61 (1H, d), 7.55 (1H, dd), 7.31 (2H, d), 7.06 (1H, d), 2.65 (2H, t), 1.68 (2H, sxt), 0.96 (3H, t)

IR (KBr) ν_{max}/cm^{-1} 2966, 2225, 1505, 1463, 1118, 818, 794, 738

MS *m/z* 261(M^+), 232(100%), 202, 176, 58

Example 10

Preparation of 2-(4-Pentylphenyl)-5-cyanobenzo[b]furan Compound 27 in Table 1

Compound 27 was prepared and purified in a similar manner to that described in Example 1 step 4 using the following reagents:

1-bromo-4-pentylbenzene obtained as described in Example 3 step 1 (1.1 g, 5 mmol), 5-cycanobenzo[b] (1.1 g, 6 mmol), sodium carbonate (1.3 g, 13 mmol), tetrakis(triphenylphosphine)palladium(0) (0.3 g, 0.3 mmol). Colourless crystals were obtained.

Yield 0.2 g (14%).

Purity (hplc) >99%.

Transitions (°C) K 99.7 (86.5 N) Iso.

^{1}**H NMR** CD_2Cl_2/δ	7.92 (1H, dd), 7.89 (2H, d), 7.61 (1H, d), 7.55 (1H, dd), 7.31 (2H, d), 7.05 (1H, d), 2.66 (2H, t), 1.65 (2H, qui), 1.35 (4H, m), 0.90 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2933, 2865, 2224, 1504, 1461, 1185, 1115, 890, 800, 740
MS *m/z*	289(M^+), (100%), 245, 232, 202, 219, 203

Example 11

Preparation of Compound 13 in Table 1

Step 1

Preparation of Methyl 3-chloromethyl-4-hydroxybenzoate

A suspension of methyl 4-hydroxybenzoate (15.2 g, 100 mmol) in hydrochloric acid (conc, 130 ml) was cooled (5 °C) with stirring. Paraformaldehyde (3.3 g, 11 mmol) was then added, and the mixture was heated (50-55 °C). The mixture was left to stand overnight. The solid was then filtered off and washed with water. The crude product was dried overnight *in vacuo* ($CaCl_2$), and recrystallised ($CHCl_3$).

A white solid was obtained.

Yield 8.0 g (40%), mp 144-145 °C, (lit.[3] 147-149 °C).

^{1}H NMR $CDCl_3/\delta$	8.03 (1H, d), 7.93 (1H, dd), 6.90 (1H, d), 6.18 (1H, s), 4.68 (2H, s), 3.90 (3H, s)
IR (KBr) ν_{max}/cm^{-1}	3241, 2958, 1688, 1605, 1287, 1152, 844, 754, 705
MS *m/z*	200(M^+), 165(100%), 149, 133, 119

Step 2

Preparation of 2-Hydroxy-5-(methoxycarbonyl)benzyltriphenylphosphonium chloride

A mixture of the product of step 1 (7.9 g, 39 mmol) and triphenylphosphine (9.8 g, 37 mmol) in chloroform (100 ml) was refluxed (1 h). The mixture was allowed to cool and the solvent was removed *in vacuo*. The residue was washed with toluene, whence it solidified. After filtering off the toluene the product heated *in vacuo* (100 °C, 1h) and recrystallised (H_2O). Colourless crystals were obtained.

Yield 13.8 g (81%), mp 256-7 °C.

^{1}H NMR $CDCl_3/\delta$	11.37 (1H, s), 7.76 (3H, dt), 7.66 (1H, ddd), 7.59 (12H, m) 7.38 (1H, d), 7.38 (1H, d), 4.71 (2H, d), 3.76 (3H, s)
IR (KBr) ν_{max}/cm^{-1}	3400, 1693, 1606, 1435, 1291, 1113, 770, 745, 690
MS *m/z*	426(M^+ -Cl^-), 395, 349, 262(100%), 183

Step 3

Preparation of Methyl 2-(4-heptylphenyl)benzo[b]furan-5-carboxylate (Compound 11 in Table 1)

N,N'-Dicyclohexylcarbodiimide (1.8 g, 9 mmol) in dry dichloromethane (20 ml) was added to a stirred mixture of 4-*N,N*-(dimethylamino)pyridine (0.2 g, 1.6 mmol), the product of step 2 (3.2 g, 6.8 mmol) and 4-heptylbenzoic acid (1.8 g, 8 mmol), in dry dichloromethane (80 ml). Stirring was continued (24 h), and dry toluene (350 ml) was added. The

dichloromethane was distilled of in a stream of nitrogen. Dry triethylamine (2.0 g, 20 mmol) was added and the mixture was heated (85 °C) with stirring under nitrogen (14 h). Tlc analysis indicated a complete reaction. After allowing to cool, the mixture was filtered and the solvent removed *in vacuo*. The residue was then flash chromatographed [silica gel / petroleum fraction (bp 40-60 °C), dichloromethane 6:4], and recrystallised (hexane).

Colourless plate-like crystals were obtained.

Yield 1.3 g (55%).

Transitions (°C) K 101 SmF 104.5 SmA 114.9 Iso.

^{1}**H NMR** CD_2Cl_2/δ	8.30 (1H, dd), 7.98 (1H, dd), 7.79 (2H, d), 7.55 (1H, d), 7.30 (2H, d), 7.07 (1H, d), 3.92 (3H, s), 2.66 (2H, s), 1.62 (2H, qui), 1.32 (8H, m), 0.89 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2927, 2852, 1717, 1590, 1300, 1160, 1086, 838, 766
MS *m/z*	350(M^+), 319, 278, 265(100%), 206

Example 12

Preparation of 2-(4-Heptylphenyl)benzo[b]furan-5-carboxylic acid (Compound 43 in Table 1)

Compound 43 was prepared and purified in a similar manner to that described in Example 1 step 5 using the following reagents:

Compound 24 obtained as described in Example 40 step 3 (4.2 g, 12 mmol), potassium hydroxide (1.4 g, 24 mmol).

Colourless needle-like crystals were obtained.

Yield 3.7 g (92%).

Transitions (°C) K 200.3 SmC 255.8 Iso

^{1}**H NMR** DMSO-d^6/δ	12.87 (1H, s), 8.25 (1H, s), 7.90 (1H, d), 7.83 (2H, d), 7.68 (1H, d), 7.47 (1H, s), 7.34 (2H, d), 2.61 (2H, t), 1.59 (2H, qui), 1.26 (8H, m), 0.85 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	3450, 2926, 2849, 2361, 1674, 1612, 1507,

	1168, 912, 836
MS *m/z*	336(M^+), 264, 251(100%), 206, 178

Example 13

Preparation of 2-(4-heptylphenyl)benzo[b]furan-5-carboxamide (Compound 44 in Table 1)

Compound 44 was prepared and purified in a similar manner to that described in Example 1 step 6 from the following reagents: Compound 43 (Example 12) (1.0 g, 3 mmol), thionyl chloride (1.1 g, 9 mmol), ammonia, (d 0.880, 2.0 ml).

A white solid was obtained.

Yield 0.6 g (60%), mp 242-243 °C.

^{1}**H NMR** DMSO-d^6/δ	8.10 (1H, d), 7.78 (2H, d), 7.77 (1H, d), 7.54 (1H, d), 7.28 (2H, d), 6.81 (1H, s), 5.85 (1H, s), 2.64 (2H, t), 1.63 (2H, qui), 1.25 (8H, m), 0.87 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	3419, 3192, 2922, 1646, 1608, 1391, 912, 801
MS *m/z*	335(M^+), 250(100%), 217, 206, 178

Example 14

Preparation of Compound 54 in Table 1 (2-(4-Heptylphenyl)-5-cyanobenzo[b]furan)

Compound 54 was prepared and purified in a similar manner to that described in Example 1 step 7 from the following reagents: Compound 44 (Example 13) (0.6 g, 1.6 mmol), thionyl chloride (1.9 g, 16 mmol).

Colourless crystals were obtained.

Yield 0.2 g (39%).

Purity (hplc) >99.9%.

Transitions (°C) K 86.5 N 87.5 Iso.

^{1}**H NMR** CD_2Cl_2/δ	7.92 (1H, d), 7.79 (2H, d), 7.61 (1H, d), 7.55 (1H, dd), 7.31 (2H, d), 7.05 (1H, s), 2.66 (2H, t), 1.65 (2H, qui), 1.30 (8H, m), 0.89 (3H, t)

IR (KBr) ν_{max}/cm^{-1}	2920, 2840, 2229, 1616, 1504, 1119, 881, 741
MS *m/z*	317(M^+), 245, 232(100%), 203, 176

Example 15

Preparation of Compound 45 in Table 1 (Methyl 2-(4-nonyloxyphenyl)benzo[b]furan-5-carboxylate)

A suspension of 4-nonyloxybenzoic acid (3.2 g, 12 mmol) in thionyl chloride (16.4 g, 138 mmol) was stirred overnight with exclusion of moisture. The solution was then refluxed (1 h), and allowed to cool. The excess thionyl chloride was removed in vacuo. Residual hydrogen chloride was removed by repeated addition of dry toluene, followed by removal in vacuo. The acid chloride was then added to 2-hydroxy-5-(methoxycarbonyl)benzyltriphenylphophonium chloride obtained as described in Example 11 step 2 (4.6 g, 10 mmol) and dry triethylamine (3.0 g, 30 mmol) in dry toluene (45 ml), and the mixture was refluxed (18 h) with stirring under nitrogen. The reaction was monitored by tlc analysis. The mixture was allowed to cool, the precipitate of triethylammonium chloride was filtered off, and the solvent was removed in vacuo. The product was purified by flash chromatography [silica gel / petroleum fraction (bp 40-60 °C), dichloromethane 7:3], followed by recrystallization (hexane).

A white solid was obtained.

Yield 0.9 g (22%).

Transitions (°C) K 151.5 SmA 152.0 Iso.

^{1}**H NMR** CD_2Cl_2/δ	8.19 (1H, d), 7.87 (1H, dd), 7.72 (2H, d), 7.45 (1H, d), 6.90 (2H, d), 6.89 (1H, s), 3.93 (2H, t), 3.83 (3H s), 1.72 (2H, qui), 1.39 (2H, qui), 1.22 (10H, m), 0.81 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2920, 1722, 1612, 1506, 766
MS *m/z*	394(M^+), 268(100%), 237, 210, 182

Example 16

Preparation of 2-(4-Nonyloxylphenyl)benzo[b]furan-5-carboxylic acid (Compound 46 in Table 1)

Compound 46 was prepared and purified in a similar manner to that described in Example 1 step 5 from the following reagents: Compound 45 obtained as described in Example 15 (0.8 g, 1.9 mmol), potassium hydroxide (0.2 g, 4 mmol).

A white crystalline solid was obtained.

Yield 0.6 g (86%).

Transitions (°C) K 172 SmC 193.2 N 253.7 Iso.

^{1}H NMR CD_2Cl_2, DMSO-d^6/δ	8.27 (1H, d), 7.97 (1H, dd), 7.81 (2H, d), 7.52 (1H, d), 7.00 (1H, d), 6.99 (2H, d), 4.02 (2H, t), 3.50 (1H, s), 1.80 (2H, t), 1.48 (2H, m), 1.27 (10H, m), 0.89 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	3450, 2920, 2857, 1679, 1615, 1504, 802, 769
MS *m/z*	380(M^+), 363, 336, 254(100%), 225

Example 17

Preparation of 2-(4-Nonyloxylphenyl)benzo[b]furan-5-carboxamide (Compound 47 in Table 1)

Compound 47 was prepared and purified in a similar manner to that described in Example 1 step 6 using the following reagents:

Compound 46 obtained as described in Example 16 (0.5 g, 1.4 mmol), thionyl chloride (0.5 g, 4 mmol), ammonia, (d 0.880, 1.0 ml).

A white solid was obtained.

Yield 0.2 g (38%).

Transitions (°C) K 225 N 235 Iso.

^{1}H NMR $CDCl_3$/δ	8.15 (1H, s), 7.83 (1H, d), 7.80 (2H, d), 7.62 (1H, s), 7.51 (1H, d), 6.99 (2H, d), 6.98 (1H, s), 6.53 (1H, s), 4.02 (2H, t), 1.81 (2H, qui), 1.42 (2H, m), 1.28 (10H, m), 0.89

(3H, t)

IR (KBr) ν_{max}/cm^{-1} 3440, 3200, 2919, 2850, 1645, 1611, 1504, 835, 807, 770

MS *m/z* 379(M^+), 350, 336, 254(100%), 238

Example 18

Preparation of 2-(4-Nonyloxyphenyl)-5-cyanobenzo[b]furan (Compound 16 in Table 1)

Compound 16 was prepared and purified in a similar manner to that described in Example 1 step 7 using the following reagents.

Compound 47 from Example 17 (0.2 g, 0.5 mmol), thionyl chloride (0.6 g, 5 mmol).

A white solid was obtained.

Yield 0.04 g (22%).

Purity (hplc) 96.6%.

Transitions (°C) K 103.0 SmA 119.7 Iso.

^{1}**H NMR** CD_2Cl_2/δ 7.90 (1H, dd), 7.80 (2H, d), 7.59 (1H, d), 7.53 (1H, dd), 7.00 (2H, d), 6.96 (1H, d), 4.02 2H, t), 1.80 (2H, qui), 1.47 (2H, m), 1.34-1.26 (10H, m), 0.89 (3H, t)

IR (KBr) ν_{max}/cm^{-1} 2921, 2850, 2225, 1609, 1504, 1175, 1010, 875, 802

MS *m/z* 361(M^+), 235(100%), 206, 190, 164

Example 19

Preparation of Compound 48 in Table 1

Step 1

Preparation of Benzonitrile-4-boronic acid

Benzonitrile-4-boronic acid was prepared and purified in a similar manner to that described in Example 9 step 4 using the following reagents:

4-Bromobenzonitrile (25.0 g, 37 mmol), n-butyllithium (2.5M in hexanes, 57.5 ml, 44 mmol), trimethyl borate (28.5 g, 274 mmol).

Benzonitrile-4-boronic acid from step 1(0.2 g, 1.5 mmol), 2-heptyl-5-bromobenzo[b]furan from step 2 (0.4 g, 1.4 mmol), sodium carbonate (0.4 g, 3.5 mmol), tetrakis(triphenylphosphine)palladium(0) (0.05 g, 0.04 mmol). A white solid was obtained.

Yield 0.03 g (7%).

Purity (hplc) 90.5%.

Transitions (°C) K 43.0 (30.9 N) Iso.

^{1}**H NMR** CD_2Cl_2/δ	7.71 (5H, m), 7.47 (1H, d), 7.43 (1H, dd), 6.45 (1H, d), 2.77 (2H, t), 1.74 (2H, qui), 1.33 (8H, m), 0.87 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2934, 2861, 2229, 1608, 1468, 844, 808
MS *m/z*	317(M^+), 274, 260, 232(100%), 190

Example 20

Preparation of Compound 28 in Table 1

Step 1

Preparation of 1-Bromo-4′-pentylbiphenyl

4-Bromobiphenyl (35.0 g, 150 mmol), valeryl chloride (21.8 g, 181 mmol), aluminium chloride (22.0 g, 164 mmol), poly(methylhydrosiloxane) (24.0 g, 399 mmol) were reacted using a method analogous to that described in Example 1 step 1 except that dry 1,2-dichloroethane (600 ml) was used in place of dry dichloromethane. The title product was recrystallised from ethanol.

A pale-brown solid was obtained.

Yield 21.1 g (46%), mp 94-96 °C (lit.[Jawdosiuk, 1977 #157] 95-96 °C).

^{1}**H NMR** CD_2Cl_2/δ	7.56 (2H, d), 7.49 (2H, d), 7.48 (2H, d), 7.27 (2H, d), 2.64 (2H, t), 2.64 (2H, t), 1.65 (2H, qui), 1.36 (4H, m), 0.90 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2931, 2865, 1690, 1137, 1079, 803, 502
MS *m/z*	304,302(M^+), 247(100%)165, 152, 139

Step 2

Preparation of 4'-Pentylbiphenylboronic acid

n-Butyllithium (2.5M in hexanes, 231 ml, 577 mmol) was added dropwise to a stirred solution of the product of step 1 in dry tetrahydrofuran (90 ml) at -70 °C under nitrogen. Stirring under nitrogen was continued (30 min) and trimethyl borate (6.9 g, 66 mmol) was added dropwise, maintaining the temperature below -10 °C. The system was allowed to return to room temperature with stirring under nitrogen. Hydrochloric acid (5M, 14 ml) was then added with stirring. The mixture was poured into water and ether added. The separated aqueous layer was washed with ether (2 x 200 ml) and the combined organic layers were washed with water and brine, dried ($MgSO_4$), and the solvent removed *in vacuo*.

A light-brown solid was obtained.

Yield 7.2 g (81%).

MS *m/z* 268(M^+), 224, 183(100%), 167, 152

Step 3

Preparation of 2-Cyano-5-(4'-pentylbiphenyl)benzo[b]furan (Compound 28)

2-Cyano-5-bromobenzo[b]furan obtained as described in Example 2 step 3 (0.6 g, 2.7 mmol) and sodium carbonate (0.7 g, 6.8 mmol) in 1,2-dimethoxyethane (5 ml), were stirred under nitrogen. Tetrakis(triphenylphosphine)palladium(0) (0.3 g, 0.3 mmol) was added, followed by the product of step 2 (1.1 g, 4.1 mmol) in 1,2-dimethoxyethane (10 ml), and the mixture heated (80 °C) with stirring under nitrogen (4 h). Completion of the reaction was indicated by glc and tlc analysis. After allowing to cool, the reaction mixture was poured into water and ether added. The separated aqueous layer was washed with ether (2 x 100 ml), and the combined ethereal layers washed with brine and dried ($MgSO_4$). After removal of the solvent *in vacuo* the residue was purified by flash chromatography [silica gel / petroleum fraction (bp 40-60 °C) (impurity); petroleum fraction (bp 40-60

°C), dichloromethane 7:3 (product)]. The desired product was then recrystallised (hexane).

Colourless needle-like crystals were obtained.

Yield 0.1 g (10%).

Purity (hplc) 99.9%.

Transitions (°C) K 134.0 B 147.3 N 255.6 Iso.

^{1}**H NMR** CD_2Cl_2/δ	7.94 (1H, dd), 7.82 (1H, dd), 7.71 (2H, d), 7.69 (2H, d), 7.66 (1H, ddd), 7.58 (2H, d), 7.57 (1H, d), 7.29 (2H, d), 2.66 (2H, t), 1.66 (2H, qui), 1.36 (4H, m), 0.92 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2931, 2862, 2237, 1505, 1179, 949, 805
MS *m/z*	365(M^+), (100%), 346, 308, 252, 58

Example 21

Preparation of Compound 29 in Table 1

Step 1

Preparation of 2-(4'-Pentylbiphenyl)-5-cyanobenzo[b]furan

Compound 29 was prepared and purified in a similar manner to that described in Example 1 step 4 using the following reagents:

1-Bromo-4'-pentylbiphenyl (Example 20 step 1) (1.5 g, 5 mmol), 5-cyanobenzo[b]furan-2-boronic acid (Example 9 step 40 (1.5 g, 8 mmol), sodium carbonate (1.3 g, 13 mmol), tetrakis(triphenylphosphine)palladium(0) (0.6 g, 0.6 mmol)

The product was recrystallised from ethanol / dichloromethane 5:1.

A white crystalline solid was obtained.

Yield 0.3 g (16%).

Purity (hplc) >99%.

Transitions (°C) K 187.1 N 284.2 Iso.

^{1}**H NMR** CD_2Cl_2/δ	7.96 (1H, d), 7.95 (2H, d), 7.73 (2H, d), 7.63 (1H, d), 7.58 (2H, d), 7.56 (1H, dd), 7.30 (2H, d), 7.13 (1H, d), 2.66 (2H, t), 1.66 (2H, qui), 1.36 (4H, m), 0.91 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2933, 2859, 2229, 1497, 1122, 913, 803, 746

MS *m/z* 365(M^+), 308, 277, 165, 43(100%)

Example 22

Preparation of Compound 49 in Table 1

Step 1

Preparation of 5-Bromobenzo[b]furan-2-boronic acid

Dry diisopropylamine (2.0 g, 20 mmol) was added to n-butyllithium (2.5M in hexanes, 8 ml, 20 mmol) at -10 °C, and the mixture was stirred under nitrogen (20 min). 5-Bromobenzo[b]furan obtained as described in Example 9 step 2 (3.5 g, 18 mmol) in dry ether (35 ml) was added and the mixture stirred (2 h) at -10 °C under nitrogen. Trimethyl borate (3.7 g, 36 mmol) was added maintaining low temperature, and the mixture was allowed to return to room temperature with stirring under nitrogen. Hydrochloric acid (5M, 15 ml) was added with stirring. The mixture was then poured into water and ether added. The separated aqueous layer was washed with ether (2 x 50 ml) and the combined organic layers were washed with sodium hydroxide solution (10%, 30 ml). The separated aqueous layer was washed with light petroleum (40-60 °C fraction) and acidified to pH3 with hydrochloric acid (5M). It was then washed with ether (2 x 50 ml). The combined organic layers were washed with water and brine, dried ($MgSO_4$), and the solvent removed *in vacuo*.

A pale-orange solid was obtained.

Yield 3.4 g (78%).

^{1}H NMR DMSO-d^6/δ 8.62 (2H, s), 7.92 (1H, d), 7.56 (1H, d), 7.46 (1H, dd), 7.42 (1H, s)

MS *m/z* 196(M^+-$B(OH)_2$), 165, 151, 117, 89(100%),

Step 2

Preparation of 1-Iodo-4-pentylbenzene

1-Iodo-4-pentylbenzene was prepared and purified in a similar manner to that described in Example 1 step 1 using the following reagents:

Iodobenzene (20.4 g, 100 mmol), valeryl chloride (14.5 g, 120 mmol), aluminium chloride (14.7 g, 110 mmol), poly(methylhydrosiloxane) (16.0 g 267 mmol).
A pale-yellow liquid was obtained.

Yield 14.4 g (53%), bp 105 °C at 0.01 mm Hg.

^{1}H NMR $CDCl_3/\delta$	7.58 (2H, d), 6.93 (2H, d), 2.54 (2H, t), 1.58 (2H, m), 1.31 (4H, m), 0.89 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2962, 2862, 1486, 1118, 1065, 825, 795
MS *m/z*	274(M^+), 217(100%), 203, 175, 89

<u>Step 3</u>

<u>Preparation of 2-(4-pentylphenyl)-5-bromobenzo[b]furan (Compound 49 in Table 1)</u>

Compound 49 was prepared and purified in a similar manner to that described in Example 1 step 4 using the following reagents:
1-Iodo-4-pentylbenzene from step 2(3 g, 11 mmol), 5-bromobenzo[b]furan-2-boronic acid from step 1(1.3 g, 5 mmol), sodium carbonate (1.4 g, 13.5 mmol), tetrakis(triphenylphosphine)palladium(0) (0.3 g, 0.3 mmol)
The product was recrystallised from hexane.
A white crystalline product was obtained.

Yield 0.3 g (16%), mp 147-150 °C.

^{1}H NMR CD_2Cl_2/δ	7.765 (2H, d), 7.71 (1H, dd), 7.41 (1H, d), 7.36 (1H, dd), 7.28 (2H, d), 6.96 (1H, d), 2.66 (2H, t), 1.65 (2H, qui), 1.34 (4H, m), 0.90 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2932, 2860, 1610, 1583, 1162, 873, 795, 670, 508
MS *m/z*	344,342(M^+), 287(100%), 274, 206, 152

Example 23

Preparation of Compound 50 in Table 1 (2-(4-pentylphenyl)-5-(4′-cyanophenyl)benzo[b]furan)

Compound 50 was prepared in a similar manner to that described in Example 1 step 4 using the following reagents:d.

Compound 49 (Example 22) (0.3 g, 0.9 mmol), benzonitrile-4-boronic acid (Example 19 step 1)(0.2 g, 1.0 mmol), sodium carbonate (0.2 g, 2 mmol), tetrakis(triphenylphosphine)palladium(0) (0.03 g, 0.03 mmol)

The product was purified by flash chromatography [silica gel / hexane, propionitrile 40:1], followed by recrystallisation (ethanol).

A white solid was obtained.

Yield 0.04 g (12%).

Purity (hplc) 98%.

Transitions (°C) K 133.8 N 230.5 Iso.

^{1}**H NMR** CD_2Cl_2/δ	7.74 1H, d), 7.73 (2H, d), 7.68 (4H, s), 7.53 (1H, d), 7.45 (1H, dd), 7.23 (2H, d), 6.99 (1H, d), 2.58 (2H, t), 1.58 (2H, qui), 1.27 (4H, m), 0.83 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2927, 2854, 2226, 1607, 1463, 1153, 1125, 889, 841, 813
MS *m/z*	365(M^+), 308(100%), 264, 176, 154

Example 24

Preparation of Compound 35 in Table 1

Step 1

Preparation of 5-(4-Pentylphenyl)benzo[b]furan

5-(4-Pentylphenyl)benzo[b]furan was prepared in a similar manner to that described in Example 1 step 4 from the following reagents:

5-Bromobenzo[b]furan (Example 9 step 20 (2.5 g, 13 mmol), 4-pentylbenzeneboronic acid (Example 3 step 2) (2.9 g, 15 mmol), sodium carbonate (3.5 g, 33 mmol), tetrakis(triphenylphosphine)palladium(0) (0.5 g, 0.5 mmol)

The product was purified by flash chromatography [silica gel / petroleum fraction (bp 40-60 °C)], followed by recrystallisation (hexane).
Colourless plate-like crystals were obtained.

Yield 1.2 g (35%), mp 62-64 °C.

^{1}H NMR CD_2Cl_2/δ	7.54 (2H, d), 7.53 (1H, d), 7.52 (1H, dd), 7.27 (2H, d), 6.84 (1H, dd), 2.65 (2H, t), 1.66 (2H, qui), 1.36 (4H, m), 0.91 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2958, 2931, 2858, 1516, 1131, 885, 845, 806, 771, 743
MS *m/z*	264(M^+), 207(100%), 178, 165, 152

Step 2

Preparation of 5-(4-Pentylphenyl)benzo[b]furan-2-boronic acid

5-(4-Pentylphenyl)benzo[b]furan-2-boronic acid was prepared and purified in a similar manner to that described in Example 20 step 2 from the following reagents:
5-(4-Pentylphenyl)benzo[b]furan from step 1 (1.2 g, 5 mmol), n-butyllithium (2.5M in hexanes, 2 ml, 5 mmol), trimethyl borate (0.9 g, 9 mmol).
A pale-pink solid was obtained.

Yield 1.2 g (84%).

MS *m/z* 264(M^+-$B(OH)_2$), 207(100%), 177, 151, 127

Step 3

Preparation of 2-(4-Cyanophenyl)-5-(4′-pentylphenyl)benzo[b]furan (Compound 35 in Table 1)

Compound 35 was prepared and purified in a similar manner to that described in Example 20 step 3 from the following reagents:
Benzonitril-4-boronic acid (example 19 step 1) (0.7 g, 4 mmol), the product of step 2 above (1.1 g, 4 mmol), sodium carbonate (1.1 g, 10 mmol), tetrakis(triphenylphosphine)palladium(0) (0.2 g, 0.2 mmol).
The product was recrystallised from carbon tetrachloride.

Colourless, rhombic crystals were obtained.

Yield 0.4 g (30%).

Purity (hplc) 99.9%.

Transitions (°C) K 139.0 N 252.6 Iso

^{1}H NMR CD_2Cl_2/δ 7.99 (2H, d), 7.83 (1H, dd), 7.76 (2H, d), 7.62-7.57 (2H, m), 7.55 (2H, d), 7.29 (2H, d), 7.27 (2H, d), 2.66 (2H, t), 1.66 (2H, qui), 1.38-1.34 (4H, m), 0.92 (3H, t)

IR (KBr) ν_{max}/cm^{-1} 2968, 2854, 2224, 1607, 1155, 842, 802

MS *m/z* 365(M^+), 308(100%), 277, 252, 154

Example 25

Preparation of Compound 51 in Table 1

Step 1

Preparation of 2-(4-Pentylphenoxy)acetaldehyde dimethyl acetal

2-(4-Pentylphenoxy)acetaldehyde dimethyl acetal was prepared and purified in a similar manner to that described in Example 8 step 1 using the following reagents;. 4-Pentylphenol (9.9 g, 60 mmol), bromoacetaldehyde dimethyl acetal (12.4 g, 73 mmol), potassium carbonate (20.8 g, 151 mmol), potassium iodide (0.6 g, 4 mmol).

A pale-yellow liquid was obtained.

Yield 4.8 g (32%), bp 125 °C at 0.01 mm Hg.

^{1}H NMR CD_2Cl_2/δ 7.08 (2H, d), 6.84 (2H, d), 4.72 (1H, t), 3.99 (2H, t), 3.46 (6H, s), 2.53 (2H, t), 1.57 (2H, qui), 1.31 (4H, m), 0.88 (3H, t)

IR (KBr) ν_{max}/cm^{-1} 2936, 1616, 1514, 1247, 1139, 1081, 976, 827, 757

MS *m/z* 252(M^+), 221, 149, 107, 75(100%)

Step 2

Preparation of 5-Pentylbenzo[b]furan

5-Pentylbenzo[b]furan was prepared and purified in a similar manner to that described in Example 8 step 2 from the following reagents;

The product of step 1 above (4.8 g, 19 mmol), polyphosphoric acid (4.6 g).

A colourless liquid was obtained.

Yield 2.2 g (62%), bp 125 °C at 0.1 mm Hg.

^{1}**H NMR** CD_2Cl_2/δ	7.61 (1H, d), 7.41 (1H, s), 7.40 (1H, d), 7.13 (1H, dd), 6.74 (1H, dd), 2.70 (2H, t), 1.65 (2H, qui), 1.35 (4H, m), 0.91 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2934, 2861, 1468, 1198, 1033, 881, 812, 764, 734
MS *m/z*	188(M^+), 145, 131(100%), 115, 91

Step 3

Preparation of 5-Pentylbenzo[b]furan-2-boronic acid

The product of step 2 (2.2 g, 12 mmol), n-butyllithium (2.5M in hexanes, 5.2 ml, 13 mmol), trimethyl borate (2.59 g, 24 mmol) were reacted using a method analogous to that described in Example 20 step 2 to yield the title compound.

A pale-orange solid was obtained.

Yield 2.7 g (97%).

MS *m/z*	232(M^+), 187, 174, 146, 130(100%),

Step 4

Preparation of 4-Cyano-4′-iodobiphenyl

4-Cyano-4′-iodobiphenyl was prepared and purified in a similar manner to that described in Example 1 step 4 from the following reagents:

p-Diiodobenzene (14.7 g, 44 mmol), benzonitrile-4-boronic acid (Example 19 step 1)(5.0 g, 34 mmol), sodium carbonate (21.6 g, 204 mmol), tetrakis(triphenylphosphine)palladium(0) (3.0 g, 3 mmol).

The product was recrystallised from ethanol.

A white crystalline product was obtained.

Yield 1.0 g (10%), mp 174-176 °C (lit.[Pummerer, 1931 #158] 166 °C).

^{1}H NMR CD_2Cl_2/δ 7.83 (2H, d), 7.74 (2H, d), 7.68 (2H, d), 7.37 (2H, d)

~~**IR** (KBr) ν_{max}/cm^{-1} 2227, 1604, 1477, 997, 853, 813, 561~~

MS *m/z* 305(M^+), (100%), 178, 151, 127, 75

Step 5

Preparation of 2-(4'-Cyanobiphenyl)-5-pentylbenzo[b]furan (Compound 51 in Table 1)

Compound 51 was prepared and purified from the product of step 4 above (1.0 g, 3 mmol), the product of step 3 above (0.8 g, 4 mmol), sodium carbonate (0.9 g, 8 mmol) and tetrakis(triphenylphosphine)palladium(0) (0.1 g, 0.1 mmol) in method analogous to that described in Example 20 step 3. The product was recrystallised from ethanol. Colourless, plate-like crystals were obtained.

Yield 36 mg (2%).

Purity (hplc) 99.5%.

Transitions (°C) K 150.8 B 167.0 N 280.3 Iso.

^{1}H NMR CD_2Cl_2/δ 7.97 (2H, d), 7.79-7.75 (4H, m), 7.72 (2H, d), 7.44 (1H, d), 7.42 (1H, d), 7.15 (1H, dd), 7.09 (1H, d), 2.71 (2H, t), 1.67 (2H, qui), 1.38-1.33 (4H, m), 0.91 (3H, t)

IR (KBr) ν_{max}/cm^{-1} 2927, 2858, 2229, 1603, 1493, 1465, 1189, 825, 802

MS *m/z* 365(M^+), 322, 308(100%), 264, 154

Example 26

Preparation of Compound 52 in Table 1

Step 1

Preparation of 2-Pentyl-5-bromobenzo[b]furan

2-Pentyl-5-bromobenzo[b]furan was prepared and purified in a similar manner to that described in Example 19 step 2 using the following reagents;

5-Bromobenzo[b]furan (Example 9 step 2) (12.0 g, 61 mmol), dry diisopropylamine (6.8 g, 67 mmol), n-butyllithium (2.5M in hexanes, 26.8 ml, 67 mmol), n-pentyl iodide (24.2 g, 122 mmol). A colourless liquid was obtained.

Yield 2.6 g (16%), bp 198 °C at 0.6 mm Hg.

^{1}H NMR CD_2Cl_2/δ	7.61 (1H, dd), 7.30 (1H, d), 7.28 (1H, d), 6.36 (1H, s), 2.76 (2H, dt), 1.74 (2H, d), 1.37 (4H, m), 0.91 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2935, 2868, 1599, 1450, 1117, 1050, 948, 867, 671, 579
MS *m/z*	268,266(M^+), 251, 223, 208(100%), 116

Step 2

Preparation of 2-Pentylbenzo[b]furan-5-boronic acid

The title compound was prepared and purified from the product of step 1 (2.5 g, 9 mmol), magnesium (0.3 g, 11 mmol) and trimethyl borate (2.09 g, 19 mmol) in a similar manner to that described in Example 1 step 2.

A pale-yellow solid was obtained.

Yield 1.7 g (78%).

MS *m/z*	642($3M^+$-$3H_2O$), 585, 255, 188, 131(100%)

Step 3

Preparation of 2-Pentyl-5-(4-(4′-cyano)biphenyl)benzo[b]furan (Compound 52 in Table 1)

Compound 52 was prepared and purified in a similar manner to that described in Example 1 step 4 from the product of step 3 above (1.7 g, 7 mmol), 4-cyano-4′-iodobiphenyl (Example 25 step

2) (1.7 g, 6 mmol), sodium carbonate (1.5 g, 14 mmol), and tetrakis(triphenylphosphine)palladium(0) (0.2 g, 0.2 mmol). The reaction was carried out with exclusion of light.

A white crystalline solid was obtained.

Yield 0.1 g (5%).

Purity (hplc) 97.6%.

Transitions (°C) K 94.8 N 236.7 Iso.

^{1}**H NMR** CD_2Cl_2/δ	7.77-7.68 (9H, m), 7.48 (1H, dd), 7.47 (1H, d), 6.45 (1H, s), 2.78 (2H, t), 1.76 (2H, qui), 1.40-1.34 (4H, m), 0.90 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2935, 2860, 2228, 1604, 1466, 1120, 948, 829, 802
MS *m/z*	365(M^+), 350, 322, 308(100%), 278

Example 27

Preparation of Compound 53 in Table 1

Step 1

Preparation of Benzo[b]furan-5-boronic acid

Benzo[b]furan-5-boronic acid was prepared and purified from 5-bromobenzo[b]furan (Example 9 step 2) (2.0 g, 10 mmol), magnesium (0.3 g, 12 mmol) and trimethyl borate (2.1 g, 20 mmol)in a similar manner to that described in Example 1 step 2. A light-brown solid was obtained.

Yield 0.7 g (43%)

MS *m/z*	432($3M^+$-$3H_2O$), 144(100%), 117, 89, 63

Step 2

Preparation of 4-(4'-Pentylcyclohexyl)phenyl trifluoromethanesulphonate

Trifluoromethanesulphonic anhydride (6.5 g, 23 mmol) was added dropwise to a stirred, cooled (0 °C) solution of 4-(*trans*-n-yentylcyclohexyl)phenol (5.0 g, 20 mmol) in dry pyridine (80 ml) under dry nitrogen. The mixture was stirred at room temperature overnight. It was then poured into water and ether added. The separated aqueous layer was washed with ether (2 x

100 ml). The combined organic layers were washed with water, hydrochloric acid (10%) (twice), and brine, dried ($MgSO_4$), and the solvent removed *in vacuo*. The product was purified by flash chromatography [silica gel / petroleum fraction (bp 40-60 °C), dichloromethane 7:3]

~~A pale yellow oil was obtained.~~

Yield 5.2 g (69%).

^{1}**H NMR** CD_2Cl_2/δ	7.21 (2H, d), 7.10 (2H, d), 2.44 (1H, tt), 1.82-1.81 (2H, m), 1.78-1.77 (2H, m), 1.38-1.36 (1H, m), 1.34-1.31 (1H, m), 1.26-1.12 (9H, m), 1.02-0.99 (1H, m), 0.96-0.93 (1H, m), 0.81 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2929, 2858, 1503, 1427, 1143, 1018, 837, 740, 607
MS *m/z*	378(M^+), 307, 252, 175, 69(100%)

Step 3

Preparation of 5-(4′-Pentylcyclohexyl-4-phenyl)benzo[b]furan

5-(4′-Pentylcyclohexyl-4-phenyl)benzo[b]furan, a compound of formula (IXA), was prepared and purified in a similar manner to that described in Example 1 step 4 from the following reagents: the product of step 2 above (3.4 g, 9 mmol), the product of step 1 above (1.6 g, 10 mmol), sodium carbonate (2.4 g, 23 mmol), tetrakis(triphenylphosphine)palladium(0) (0.3 g, 0.3 mmol)

Volatiles were removed by heating (95 °C) *in vacuo* (12 h).

A white solid was obtained.

Yield 1.9 g (61%).

Transitions (°C) K 116.3 N 153.7 Iso.

^{1}**H NMR** CD_2Cl_2/δ	7.80-7.79 (1H, m), 7.67 (1H, d), 7.56-7.51 (4H, m), 7.30 (2H, d), 6.84 (1H, dd), 2.53 (1H, tt), 1.94-1.88 (4H, m), 1.48 (2H, ddd), 1.35-1.22 (9H, m), 1.08 (2H, ddd), 0.91 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	3124, 2924, 2853, 1463, 1131, 1027, 883,

	742, 697
MS *m/z*	346(M^+), 331, 303, 275, 233(100%)

Step 4

Preparation of 5-(4'-Pentylcyclohexyl-4-phenyl)benzo[b]furan2-carboxylic acid (Compound 53)

Compound 53 was prepared and purified from the product of step 3 (1.9 g, 5.5 mmol) and n-butyllithium (2.5M in hexanes, 2.4 ml, 6.1 mmol) in a similar manner to that described for in Example 8 step 3.

A white solid was obtained.

Yield 2.0 g (79%).

Transitions (°C) K 183 N 299 Iso.

^{1}**H NMR** CD_2Cl_2/δ	7.79 (1H, dd), 7.59 (1H, dd), 7.54 (1H, d), 7.47 (2H, d), 7.45 (1H, d), 7.23 (2H, d), 2.45-2.42 (1H, m), 1.85-1.80 (4H, m), 1.43 (2H, ddd), 1.27-1.13 (9H, m), 1.00 (2H, ddd), 0.82 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2929, 2853, 1691, 1566, 1173, 813
MS *m/z*	390(M^+), (100%), 346, 333, 264, 189

Example 28

Preparation of Compound 54 in Table 1(5-(4'-Pentylcyclohexyl-4-phenyl)benzo[b]furan2-carboxamide)

Compound 54 was prepared and purified in a similar manner to that described in Example 1 step 6 using the following reagents:

Compound 53 (Example 27) (2.0 g, 4.3 mmol), thionyl chloride (1.5 g, 13 mmol), ammonia, (d 0.880, 2.9 ml).

Fibrous white needle-like crystals were obtained.

Yield 1.1 g (66%).

Transitions (°C) K 275 N 296 Iso.

^{1}**H NMR** CD_2Cl_2/δ, DMSO-d^6/δ	7.83 (1H, d), 7.63 (1H, dd), 7.56 (1H, d), 7.53 (2H, d), 7.46 1H, d), 6.92 (1H, s), 6.54 (1H, s), 2.42-

	2.35 (1H, m), 1.91-1.85 (4H, m), 1.47 (2H, ddd), 1.32-1.20 (9H, m), 1.05 (2H, ddd), 0.88 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	3393, 3170, 2928, 2852, 1675, 1615, 1168, 817
MS *m/z*	389(M^+), 316, 301, 250, 58(100%)

Example 29

Preparation of 2-Cyano-5-(4'-trans-pentylcyclohexyl-4-phenyl)benzo[b]furan (Compound 54 in Table 1)

Compound 54 was prepared and purified in a similar manner to that described in Example 1 step 7 from compound 54 (Example 28) (1.0 g, 2.6 mmol) and thionyl chloride (3.2 g, 26 mmol). The product was recrystallised from ethanol.

Yield 0.5 g (52%).

Purity (hplc) >99%.

Transitions (°C) K 113.0 N 240.7 Iso.

^{1}**H NMR** CD_2Cl_2/δ	7.86 (1H, dd), 7.75 (1H, dd), 7.61 (1H, dt), 7.55 (1H, d), 7.54 (2H, d), 7.32 (2H, d), 2.53 (1H, tt), 1.93-1.87 (4H, m), 1.56-1.44 (4H, m), 1.35-1.19 (7H, m), 1.08 (2H, m), 0.90 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2925, 2854, 2234, 1558, 1515, 1462, 1178, 1128, 950, 887
MS *m/z*	371(M^+)(100%), 300, 245, 232, 189

Example 30

Preparation of Compound 56 in Table 1

Step 1

Preparation of Ethyl 5-methoxybenzo[b]furan-2-carboxylate Ethyl 5-methoxybenzo[b]furan-2-carboxylate was prepared and purified from 5-methoxysalicylaldehyde (20.0 g, 131 mmol), diethyl bromomalonate (26.3 g, 110 mmol), potassium carbonate (32.5 g, 236 mmol), potassium iodide (0.9 g, 6 mmol), in a similar manner to that described in Example 1 step 3.

Colourless cubic crystals were obtained.

Yield 14.5 g (50%), mp 58-59.5 °C, bp 150 °C at 0.02 mm Hg.

^{1}**H NMR** CD_2Cl_2/δ	7.47 (1H, ddd), 7.45 (1H, d), 7.09 (1H, d), 7.06 (1H, dd), 4.39 (2H, q), 3.83 (3H, s), 1.40 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2988, 1721, 1560, 1195, 940, 846, 822
MS *m/z*	220(M^+), (100%), 205, 192, 175, 119

Step 2

Preparation of 5-Methoxybenzo[b]furan-2-carboxylic acid

The title compound was prepared and purified from the product of step 1 (14.5 g, 66 mmol) and potassium hydroxide (7.3 g, 130 mmol)in a similar manner to that described in Example 1 step 5. Colourless crystals were obtained.

Yield 6.1 g (48%).

Transitions (°C) K 208 N 221 Iso.

^{1}**H NMR** CD_2Cl_2, DMSO-d^6/δ	11.5 (1H, s), 7.41 (1H, d), 7.38 (1H, d), 7.06 (1h, d), 7.00 (1H, dd), 3.78 (3H, s)
IR (KBr) ν_{max}/cm^{-1}	2953, 1689, 1566, 1160, 943, 898, 850, 797
MS *m/z*	192(M^+)(100%), 177, 162, 149, 107

Step 3

Preparation of 5-Methoxybenzo[b]furan-2-carboxamide

The title compound was prepared and purified from the product of step 2 (6.0 g, 31 mmol), thionyl chloride (11.0 g, 93 mmol) and ammonia (d 0.880, 11.0 ml) in a similar manner to that described in Example 1 step 6.

Colourless plate-like crystals were obtained.

Yield 4.6 g (78%).

^{1}**H NMR** CD_2Cl_2/δ	7.42 (2H, d), 7.40 (1H, s), 7.11, (1H, d), 7.04 (1H, dd), 6.53 (1H, s, br), 5.94 (1H,

s, br), 3.84 (3H, s)

IR (KBr) ν_{max}/cm^{-1}	3451, 3138, 1692, 1608, 1476, 1156, 854, 833
MS *m/z*	191(M^+)(100%), 175, 159, 148, 133

Step 4

Preparation of 2-Cyano-5-methoxybenzo[b]furan

The product of step 3 (4.8 g, 25 mmol) and thionyl chloride (14.3 g, 120 mmol) were converted to the title compound in a similar manner to that described in Example 1 step 7.

The product was recrystallised from methanol.

White needle-like crystals were obtained.

Yield 1.5 g (36%), mp 79.5-80 °C.

^{1}H NMR CD_2Cl_2/δ	7.46 (1H, ddd), 7.44 (1H, dd), 7.12 (1H, dd), 7.09 (1H, d), 3.84 (3H, s)
IR (KBr) ν_{max}/cm^{-1}	2949, 2842, 2231, 1596, 1475, 1211, 1185, 949, 877, 750
MS *m/z*	173(M^+), (100%), 158, 130, 102, 75

Step 5

Preparation of 2-Cyano-5-hydroxybenzo[b]furan

A mixture of the product of step 4 (0.7 g, 4 mmol) and pyridinium chloride (4.6 g, 40 mmol) was refluxed (3 min). The reaction mixture was then poured into ice / water. The product was extracted into ether (2 x 200 ml), and the combined organic extracts were washed with water and brine and dried ($MgSO_4$), and the solvent removed *in vacuo*. The product was recrystallised from ethanol.

Colourless crystals were obtained.

Yield 0.5 g (80%).

Step 6

Preparation of 2-Cyanobenzo[b]furan-5-trans-(oxycarbonyl-4-pentylcyclohexane) (Compound 56 in Table 1)

The product of step 5 (0.5 g, 3 mmol) and *trans*-4-pentylcyclohexylcarboxylic acid (0.6 g, 3 mmol) were dissolved

in dry dichloromethane (30 ml) and (4-*N,N*-dimethylamino)pyridine (0.1 g, 1 mmol) was added, and the mixture stirred. *N,N'*-Dicyclohexylcarbodiimide (0.6 g, 3 mmol) was then added, and stirring was continued (24 h). The reaction was monitored by tlc analysis. The precipitate of *N,N'*-dicyclohexylurea was filtered off, and the solvent removed *in vacuo*. The product was purified by flash chromatography [silica gel / petroleum fraction (bp 40-60 °C), dichloromethane 7:3], followed by recrystallization (ethanol). A white crystalline solid was obtained.

Example 31

Preparation of Compound 100 in Table 2

Step 1

Preparation of 4-Bromo(2,2-dimethoxy)ethyl sulphanylbenzene

Sodium (13.8 g, 600 mmol) was added to superdry ethanol (400 ml) with stirring under nitrogen. 4-Bromothiophenol (compound **102**) (103.3 g, 546 mmol) was added and stirring was continued (5 min). Bromoacetaldehyde dimethyl acetal (120.0 g, 709 mmol) was then added and the mixture refluxed overnight with stirring under nitrogen. The mixture was then washed with dichloromethane (3 x 100 ml). The combined washings were washed with water and brine, dried ($MgSO_4$), and the solvent removed *in vacuo*. The residue was purified by distillation. A colourless oil was obtained.

Yield 104.3 g (69%) bp 132 °C at 2 mm Hg.

^{1}H NMR $CDCl_3/\delta$	7.39 (2H, d), 7.24 (2H, d), 4.5 (1H, t), 3.36 (6H, s), 3.08 (2H, d)
IR (KBr) ν_{max}/cm^{-1}	2930, 2830, 1470, 1120, 1090, 800, 480
MS *m/z*	278,276(M^+), 247, 215, 201, 189, 75(100%)

Step 2

Preparation of 5-Bromobenzo[b]thiophene

The product of step 1, (104.3 g, 376 mmol) and polyphosphoric acid (156.2 g)were converted to 5-bromobenzo[b]thiophene in Example 8 step 2. A white crystalline solid was obtained.

Yield 12.0 g (15%), mp 46-47 °C (lit[4] 47-48 °C).

^{1}H NMR CD_2Cl_2/δ	7.98 (1H, d), 7.77 (1H, d), 7.52 (1H, d), 7.44 (1H, dd), 7.30 (1H, dd)
IR (KBr) ν_{max}/cm^{-1}	3080, 1576,1399, 898, 807, 472
MS m/z	214,212(M^+), 133(100%), 106, 89, 81

Step 3

Preparation of 5-(4-Heptylphenyl)benzo[b]thiophene

The product of step 2 (4.6 g, 22 mmol), 4-heptylbenzeneboronic acid (Example 1 step 2) (5.7 g, 26 mmol), sodium carbonate (5.8 g, 55 mmol) and tetrakis(triphenylphosphine)palladium(0) (0.8 g, 0.7mmol) were treated as described in Example 1 step 4 to give the title compound. A colourless was obtained, which solidified on cooling.

Yield 4.8 g (71%), bp 225 °C at 0.01 mm Hg.

^{1}H NMR CD_2Cl_2/δ	7.95 (1H, d), 7.85 (1H, d), 7.51 (1H, dd), 7.50 (2H, d), 7.42 (1H, d), 7.31 (1H, dd), 7.20 (2H, d), 2.57 (2H, t), 1.57 (2H, qui), 1.28-1.20 (8H, m), 0.81 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2929, 2857, 1496, 1089, 899, 805, 757
MS m/z	308(M^+), 252, 223(100%), 167, 58

Step 4

Preparation of 5-(4-Heptylphenyl)benzo[b]thiophene-2-carboxylic acid (Compound 100 in Table 2)

Compound 100 was prepared and purified in a similar manner to that described in Example 8 step 3 using the following reagents:

the product of step 3 above (2.5 g, 8 mmol) and n-butyllithium (2.5M in hexanes, 3.4 ml, 9 mmol).

A white solid was obtained.

Yield 1.1 g (39%), mp 164-170 °C.

^{1}**H NMR** CD_2Cl_2,DMSO-d^6/δ	8.05 (1H, d), 8.02 (1H, s), 7.90 (1H, d), 7.68 (1H, dd), 7.55 (2H, d), 7.26 (2H, d), 2.63 (2H, t), 1.62 (2H, qui), 1.32-1.23 (8H, m), 0.86 (3H, t) (acidic proton signal was not shown)
IR (KBr) ν_{max}/cm^{-1}	3010, 2931, 2855, 1690, 1547, 1514, 1165, 803, 757, 700
MS *m/z*	352(M^+), 281, 267(100%), 221, 208

<u>Example 32</u>

<u>Preparation of 5-(4-Heptylphenyl)benzo[b]thiophene-2-carboxamide (Compound 101 in Table 2)</u>

Compound 101 was prepared and purified in a similar manner to that described in Example 1 step 6 from compound 57 (Example 31)(1.1 g, 3 mmol), thionyl chloride (1.1 g, 9 mmol) and ammonia (d 0.880, 1.1 ml).

A white crystalline solid was obtained.

Yield 1.8 g (92%), mp 204-205 °C.

^{1}**H NMR** CD_2Cl_2/δ	8.06 (1H, d,), 7.93 (1H, d), 7.81 (1H, s), 7.70 (1H, dd), 7.58 (2H, d), 7.30 (2H, d), 2.66 (2H, t), 1.65 (2H, qui), 1.36-1.26 (8H, m), 0.89 (3H, t) (H-bonded proton signals were not shown)
IR (KBr) ν_{max}/cm^{-1}	3399, 3187, 2927, 2855, 1643, 1609, 1512, 1172, 800
MS *m/z*	351(M^+), 279, 266(100%), 248, 221

Example 33

Preparation of 2-Cyano-5-(4-heptylphenyl)benzo[b]thiophene (Compound 102 in Table 2)

Compound 102 was prepared and purified in a similar manner to that described in Example 1 step 7 from Compound 61 (Example 31) (1.0 g, 3 mmol), thionyl chloride (3.3 g, 28 mmol).

A white crystalline solid was obtained.

Yield 0.4 g (43%), mp 93.2 °C.

^{1}**H NMR** CD_2Cl_2/δ 8.1 (1H, d), 7.97 (1H, d), 7.94 (1H, d), 7.80 (1H, dd), 7.57 (2H, d), 7.31 (2H, d), 2.66 (2H, t), 1.65 (2H, qui), 1.35-1.30 (8H, m), 0.89 (3H, t)

Example 34

Preparation of 4-Heptylphenyl 5-(4-heptylphenyl)benzo[b]furan-2-carboxylate (Compound 5 in Table 1)

Step 1

Preparation of 4-Heptylphenol

Hydrogen peroxide (100 vol, 387 ml, 3.39 mol) was added slowly to a stirred solution of 4-heptyl benzeneboronic acid (15.8 g, 72.0 mmol) in dry diethyl ether (100 ml) and the mixture was refluxed (2 h). After allowing to cool, the mixture was washed with ether (3 x 150 ml). The combined ethereal layers were washed with saturated sodium sulphite solution and shaken with aqueous sodium hydroxide (2M). The white precipitate was filtered off and washed with petroleum fraction (bp 40-60 °C), and then adjusted to pH 3 with hydrochloric acid (conc.). The product was extracted by washing with ether (3 x 150 ml). The combined organic layers were washed with brine and dried ($MgSO_4$), and the solvent removed *in vacuo*. The residue was purified by distillation.

A colourless liquid was obtained.

Yield 4.4 g (32 %) bp 115 °C at 0.03 mmHg (lit.[1] 65°C).

^{1}**H NMR** $CDCl_3/\delta$ 7.02 (2H, d), 6.76 (2H, d), 5.10 (1H, s),

2.53 (2H, d) 1.56 (2H, m), 1.31 (8H, m), 0.87 (3H, t)

IR (KBr) ν_{max}/cm^{-1} 3340, 2925, 1615, 1515, 1175, 830, 760

MS *m/z* 192(M^+) 120, 107, 91, 43(100%)

~~Step 2~~

Preparation of Compound 5 in Table 1

5-(4-Heptylphenyl)benzo[b]furan-2-carboxylic acid (1.0 g, 3 mmol), prepared as described in Example 1 step 5 and the product of step 1 above (0.6 g, 3 mmol) were dissolved in dry DCM (100 ml) and DMAP (0.4 g, 3 mmol) was added, and the mixture stirred. DCC (0.6 g, 3 mmol) was then added, and stirring was continued (24 h). The reaction was monitored by tlc analysis. The precipitate of dicyclohexylurea was then filtered off, and the solvent removed *in vacuo*. The product was purified by flash chromatography [silica gel / petroleum fraction (bp 40-60 °C), DCM 7:3], followed by recrystallization (hexane).

A white solid was obtained.

Yield 0.8 g (52%). Purity (hplc) 99%.

^{1}H NMR CD_2Cl_2/δ 7.91 (1H, dd), 7.75 (1H, d), 7.73 (1H, dd), 7.67 (1H, d), 7.54 (2H, d), 7.28 (2H, d), 7.25 (2H, d), 7.14 (2H, d), 2.65 (2h, t), 2.63 (2H, t), 1.64 (4H, m), 1.31 (16H, m), 0.88 (6H, t)

IR (KBr) ν_{max}/cm^{-1} 2920, 1734, 1578, 802

MS *m/z* 510(M^+), 481, 425, 319(100%), 191

Example 35

Preparation of 4-Butoxyphenyl 5-(4-heptylphenyl)benzo[b]furan-2-carboxylate (Compound 7 in Table 1)

The title compound was prepared and purified in a similar manner to that described for in Example 34 using the quantities stated.

5-(4-Heptylphenyl)benzo[b]furan-2-carboxylic acid (0.5 g, 1.5 mmol), 4-butoxyphenol (0.3 g, 1.5 mmol), DMAP (0.2 g, 1.5 mmol), DCC (0.3 g, 1.5 mmol).

The product was obtained as a white, crystalline solid.

Yield 0.4 g (52%). Purity (hplc) >98%.

^{1}**H NMR** $CDCl_3/\delta$	7.89 (1H, dd), 7.75 (1H, s), 7.72 (1H, dd), 7.67 (1H, d), 7.54 (2H, d), 7.29 (2H, d), 7.17 (2H, d), 6.95 (2H, d), 3.98 (2H, t), 2.66 (2H, t), 1.79 (2H, qui), 1.66 (2H, qui) 1.49 (2H, qui), 1.32 (8H, m), 0.99 (3H, t), 0.89 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2925, 1734, 1502, 1160, 948, 804
MS *m/z*	484(M^+), 319, 264, 166, 69(100%)

<u>Example 36</u>

<u>Preparation of 4-Hexyloxyphenyl 5-(4-heptylphenyl)benzo[b]furan-2-carboxylate (Compound 8 in Table 1)</u>

The title compound was prepared and purified in a similar manner to that described in Example 34 using the quantities stated.

5-(4-Heptylphenyl)benzo[b]furan-2-carboxylic acid (0.5 g, 1.5 mmol), 4-hexyloxyphenol (0.3 g, 1.5 mmol), DMAP (0.2 g, 1.5 mmol), DCC (0.3 g, 1.5 mmol).

A white, crystalline solid was obtained.

Yield 0.3 g (40%). Purity (hplc) >99.9%.

^{1}**H NMR** CD_2Cl_2/δ	7.93 (1H, dd), 7.77 (1H, d), 7.75 (1H, dd), 7.68 (1H, d) 7.56 (2H, d), 7.29 (2H, d), 7.16 (2H, d), 6.96 (2H, d) 3.98 (2H, t), 2.66 (2H t), 1.79 (2H, qui), 1.64 (2H, qui), 1.48 (2H, qui), 1.34 (12H, m), 0.93 (3H, t), 0.89 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2933, 2858, 1733, 1502, 1310, 1199, 1160, 1072, 948, 803
MS *m/z*	512(M^+), 482, 427, 398, 178(100%)

Example 37

Preparation of 4-Pentylphenyl 5-(4-heptylphenyl)benzo[b]furan-2-carboxylate (Compound No. 66 in Table 1)

The title compound was prepared and purified in a similar manner to that described in Example 34 using the quantities stated.

5-(4-Heptylphenyl)benzo[b]furan-2-carboxylic acid (0.5 g, 1.5 mmol), 4-pentylphenol (0.3 g, 1.5 mmol), DMAP (0.2 g, 1.5 mmol), DCC (0.3 g, 1.5 mmol).

A white, crystalline solid was obtained.

Yield 0.2 g (30%). Purity (hplc) 97.6%.

^{1}H NMR CD_2Cl_2/δ	7.93 (1H, dd), 7.77 (1H, d), 7.75 (1H, dd), 7.69 (1H, d), 7.56 (2H, d), 7.30 (2H, d), 7.27 (2H, d), 7.15 (2H, d), 2.67 (2H, t), 2.64 (2H, t), 1.65 (4H, m), 1.33 (12H, m) 0.91 (3H, t), 0.89 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2958, 2921, 2852, 1732, 1303, 1221, 1161, 803, 741
MS *m/z*	482(M^+), 397, 319(100%), 263, 178

Example 38

Preparation of (S)-(+)-4-(2-Methylbutyl)phenyl 5-(4-heptylphenyl)benzo[b]furan-2-carboxylate (Compound 11 in Table 1)

The title compound was prepared and purified in a similar manner to that described for in Example 34 using the quantities stated.

5-(4-Heptylphenyl)benzo[b]furan-2-carboxylic acid (0.5 g, 1.5 mmol), (*S*)-(+)-4-(2-methylbutyl)phenol (0.3 g, 1.5 mmol) DMAP (0.2 g, 1.5 mmol) , DCC (0.3 g, 1.5 mmol).

A white, crystalline solid was obtained.

Yield 0.5 g (75%). Purity (hplc) 99.1%.

^{1}H NMR CD_2Cl_2/δ	7.93 (1H, dd), 7.77 (1H, d), 7.75 (1H, dd), 7.69 (1H, d), 7.56 (2H, d), 7.29

	(2H, d), 7.24 (2H, d), 7.16 (2H, d), 2.68(1H, dd), 2.66 (2H, t), 2.41 (1H, dd), 1.66 (3H, m), 1.32 (10H, m), 0.93 (3H, t), 0.89(3H, t), 0.87 (3H, d)
IR (KBr) ν_{max}/cm^{-1}	2965, 2858, 1735, 1569, 1502, 1294, 1075, 950, 807, 745
MS *m/z*	482(M^+), 397, 319(100%), 267, 178
$[\alpha]_D^{26°}$	+5.0° (0.01947 g/ml)

Example 39

Preparation of (S)-(+)-1-Methylheptyl 5-(4-heptylphenyl)benzo[b]furan-2-carboxylate (Compound 62 in Table 1)

The title compound was prepared and purified in a similar manner to that described for in Example 34 using the quantities stated.

5-(4-Heptylphenyl)benzo[b]furan-2-carboxylic acid (0.5 g, 1.5 mmol), (*S*)-(+)-octan-2-ol (0.2 g, 1.5 mmol), DMAP (0.2 g, 1.5 mmol), DCC (0.3 g, 1.5 mmol).

A colourless oil was obtained.

Yield 0.5 g (74%). Purity (hplc) 99.7%.

^{1}**H NMR** CD_2Cl_2/δ	7.85 (1H, dd), 7.68 (1H, dd), 7.61 (1H, d), 7.53 (1H, d) 7.52 (2H, d), 7.27 (2H, d), 5.17 (1H, m), 2.64 (2H, t), 1.75(2H, m), 1.62 (2H, m), 1.33 (19H, m), 0.88 (3H, t), 0.87 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2929, 2856, 1719, 1539, 1461, 1245, 1165, 847, 803, 597
MS *m/z*	448(M^+), 363, 336, 251, 57(100%)
$[\alpha]_D^{23°}$	+43.3° (0.01878 g/ml)

Example 40

Preparation of Preparation of Methyl 5-(4-heptylphenyl)benzo[b]furan-2-carboxylate (Compound 24 in Table 1)

A mixture of compound Compound 43 in Table 1(0.1 g, 0.3 mmol) and sulphuric acid (conc.) (0.1 ml, 2.0 mmol) in methanol (5 ml) was refluxed (24 h) with exclusion of moisture. After allowing to cool, the mixture was poured into water (20 ml) and DCM added (20 ml) The separated aqueous layer was washed with DCM (2 x 20 ml). The combined organic layers were washed with water and brine, dried ($MgSO_4$), and the solvent removed *in vacuo*. The product was purified by recrystallization (hexane). A white crystalline solid was obtained.

Yield 0.1 g (95%). Purity (hplc) >99.5%.

^{1}H NMR CD_2Cl_2/δ 7.88 (1H, d), 7.70 (1H, dd), 7.64 (1H, d), 7.57 (1H, d), 7.53 (2H, d), 7.28 (2H, d), 3.95 (3H, s), 2.66 (2H, s), 1.65 (2H, qui), 1.32 (8H, m), 0.89 (3H, t)

IR (KBr) ν_{max}/cm^{-1} 2930, 2856, 1736, 1565, 1438, 1164, 1099, 898, 847, 767

MS *m/z* 350(M^+), 293, 265(100%), 177, 165

Example 41

Preparation of Ethyl 2-(4-heptylphenyl)benzo[b]furan-5-carboxylate (Compound 64 in Table 1)

Compound 64 was prepared and purified in a similar manner to that described for the preparation of compound 24 using the quantities stated.

Compound 63 in Table 1 (0.1 g, 0.3 mmol), sulphuric acid (conc.) (0.1 ml, 0.05 mmol), ethanol (5 ml).

Colourless needle-like crystals were obtained.

Yield 0.05 g (46%). Purity (hplc) >99%.

^{1}H NMR CD_2Cl_2/δ 8.30 (1H, d), 7.99 (1H, dd), 7.79 (2H, d), 7.55 (1H, d), 7.30 (2H, d), 7.06 (1H, d), 3.67 (2H, q), 2.66 (2H, t),1.65 (2H,

	qui), 1.14 (3H, t), 1.30 (8H, m), 0.89 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2929, 2856, 1708, 1616, 1509, 1445, 1172, 1019, 817
MS *m/z*	364(M^+), 279, 251, 203, 91(100%),

Example 42

Preparation of 4-Pentylphenyl 2-(4-heptylphenyl)benzo[b]furan-5-carboxylate (Compound 65 in Table 1)

The title compound was prepared and purified in a similar manner to that described for the preparation of compound 5 in Table 1 in Example 34 using the quantities stated.

Compound 63 in Table 1 (0.3 g, 0.9 mmol), 4-pentylphenol (0.2 g, 0.9 mmol), DCC (0.2 g, 0.9 mmol), DMAP (0.1 g, 0.9 mmol). Colourless crystals were obtained.

Yield 0.3 g (67%). Purity (hplc) 97.1%.

^{1}**H NMR** CD_2Cl_2/δ	8.46 (1H, d), 8.12 (1H, dd), 7.81 (2H, d), 7.62 1H, d), 7.31 2H, d), 7.26 (2H, d), 7.13 (2H, d), 7.11 (1H, d), 2.67 (2H, t), 2.65 (2H, t), 1.65 (4H, qui), 1.32 (14H, m), 0.91 (3H, t), 0.89 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2930, 2857, 1736, 1510, 1155, 1065, 913, 803, 761
MS *m/z*	482(M^+), 397, 369, 319(100%), 205

Example 43

Preparation of 4-Heptylphenyl 2-(4-heptylphenyl)benzo[b]furan-5-carboxylate (Compound 19 in Table 1)

The title compound was prepared and purified in a similar manner to that described for in Example 34 using the quantities stated.

Compound 63 in Table 1 (0.3 g, 0.9 mmol), 4-heptylphenol (0.2 g, 0.9 mmol), DCC (0.2 g, 0.9 mmol), DMAP (0.1 g, 0.9 mmol). A white solid was obtained.

Yield 0.3 g (65%). Purity (hplc) 99.1%.

^{1}**H NMR** CD_2Cl_2/δ	8.46 (1H, dd), 8.13 (1H, dd), 7.81 (2H, d), 7.62 (1H, d), 7.31 (2H, d), 7.26 (2H, d), 7.13 (2H, d), 7.11 (1H, d), 2.66 (2H, t), 2.65 (2H, t), 1.65 (4H, m), 1.32 (16H, m), 0.90 (3H, t), 0.89 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2929, 2857, 1737, 1510, 1465, 1156, 1065, 914, 838, 761
MS *m/z*	510(M^+), 425, 318(100%), 220, 205

Example 44

Preparation of 4-Butoxyphenyl 2-(4-heptylphenyl)benzo[b]furan-5-carboxylate (Compound 20 in Table 1)

The title compound was prepared and purified in a similar manner to that described for in Example 34 using the quantities stated.

Compound 63 in Table 1 (0.3 g, 0.9 mmol), 4-butoxyphenol (0.2 g, 0.9 mmol), DCC (0.2 g, 0.9 mmol), DMAP (0.1 g, 0.9 mmol).

A white solid was obtained.

Yield 0.3 g (69%). Purity (hplc) >99%.

^{1}**H NMR** CD_2Cl_2/δ	8.45 (1H, dd), 8.12 (1H, dd), 7.81 (2H, d), 7.62 (1H, d), 7.31 (2H, d), 7.13 (2H, d), 7.10 (1H, s), 6.94 (2H, d), 3.99 (2H, d), 2.67 (2H, t), 1.78 (2H, qui), 1.65 (2H, qui), 1.51 (2H, m), 1.30 (8H, m), 0.99 (3H, t), 0.86 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2930, 2858, 1742, 1616, 1510, 1468, 1156, 1068, 913, 803, 761
MS *m/z*	484(M^+), 399, 319(100%), 206, 57

Example 45

Preparation of 4-Hexyloxyphenyl 2-(4-heptylphenyl)benzo[b]furan-5-carboxylate (Compound 21 in Table 1)

The title compound was prepared and purified in a similar manner to that described for in Example 34 using the quantities stated.

Compound 63 in Table 1 (0.3 g, 0.9 mmol), 4-hexyloxyphenol (0.2 g, 0.9 mmol), DCC (0.2 g, 0.9 mmol), DMAP (0.1 g, 0.9 mmol).

A white solid was obtained.

Yield 0.3 g (65%). Purity (hplc) >99%.

^{1}H NMR CD_2Cl_2/δ	8.43 (1H, d), 8.10 (1H, dd), 7.79 (2H, d), 7.60 (1H, d), 7.29 (2H, d), 7.12 (2H, d), 7.08 (1H, s), 6.92 (2H, d), 3.96 (2H, t), 2.65 (2H, t), 1.77 (2H, qui), 1.63 (2H, qui), 1.46 (2H, qui), 1.30 (12H, m), 0.90 (3H, t), 0.87 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2930, 2859, 1743, 1615, 1513, 1469, 1159, 1066, 916, 835, 803
MS *m/z*	512(M^+), 483, 427, 319(100%), 291

Example 46

Preparation of (S)-(+)-4-(2-Methylbutyl)phenyl 2-(4-heptylphenyl)benzo[b]furan-5-carboxylate (Compound 22 in Table 1)

The title compound was prepared and purified in a similar manner to that described for in Example 34 using the quantities stated.

Compound 63 in Table 1 (0.3 g, 0.9 mmol), 4-(2-methyl-n-butyl)phenol (0.2 g, 0.9 mmol), DCC (0.2 g, 0.9 mmol), DMAP (0.1 g, 0.9 mmol).

White, fibrous crystals were obtained.

Yield 0.3 g (69%). Purity (hplc) 98.9%.

^{1}H NMR CD_2Cl_2/δ	8.46 (1H, d), 8.13 (1H, dd), 7.81 (2H,

	d), 7.62 (1H, d), 7.31 (2H, d), 7.23 (2H, d), 7.13 (2H, h), 7.11 (1H, d), 2.69 (3H, m), 2.41 (1H, m), 1.66 (3H, m), 1.32 (10H, m), 0.93 (3H, t), 0.89 (3H, t), 0.88 (3H, d)
IR (KBr) ν_{max}/cm^{-1}	2933, 2858, 1728, 1509, 1124, 1064, 1015, 911, 835, 798, 760
MS *m/z*	482(M^+), 397, 319(100%), 206, 57
$[\alpha]_D^{24°}$	+4.0° (0.01796 g/ml)

Example 47

Preparation of (S)-(+)-1-Methylheptyl 2-(4-heptylphenyl)benzo[b]furan-5-carboxylate (Compound 23 in Table 1)

The title compound was prepared and purified in a similar manner to that described for in Example 34 using the quantities stated.

Compound 63 in Table 1 (0.3 g, 0.9 mmol), octan-2-ol_(0.1 g, 0.9 mmol), DCC (0.2 g, 0.9 mmol), DMAP (0.1 g, 0.9 mmol).

A white crystalline solid was obtained.

Yield 0.2 g (50%). Purity (hplc) 98.7%.

^{1}**H NMR** CD_2Cl_2/δ	8.27 (1H, dd), 7.96 (1H, dd), 7.77 (2H, d), 7.52 (1H, d), 7.28 (2H, d), 7.04 (1H, d), 5.13 (1H, sxt), 2.64 (2H, t), 1.74 (2H, m), 1.61 (2H, m), 1.30 (19H, m), 0.87 (6H, m)
IR (KBr) ν_{max}/cm^{-1}	2933, 2861, 1715, 1595, 1507, 1163, 1087, 797, 765
MS *m/z*	448(M^+), 336, 319, 251, 43(100%),
$[\alpha]_D^{24°}$	+33.2° (0.03029 g/ml)

Example 48

Preparation of 2,5-Bis-(4-heptylphenyl)benzo[b]furan (Compound 66 in Table 1)

Step 1:- Preparation of 5-(4-Heptylphenyl)benzo[b]furan

The title compound was prepared in a similar manner to that described for the preparation of ethyl 5-(4-heptylphenyl)benzo{b}furan-2carboxylate in Example 1(4) using the quantities stated.

Compound 5-bromobenzofuran (10.0 g, 51 mmol), 4-heptylbenzene boronic acid (13.4 g, 61 mmol), tetrakis(triphenylphosphine)palladium(0) (0.2 g, 0.2 mmol), sodium carbonate (13.5 g, 128 mmol). The product was purified by flash chromatography [silica gel / petroleum fraction (bp 40-60 °C)], followed by recrystallisation (petroleum fraction (bp 40-60 °C))

Colourless plates were obtained.

Yield 7.5 g (50%), mp 51-3 °C

^{1}**H NMR** $CDCl_3/\delta$	7.77 (1H, d), 7.64 (1H, d), 7.55 (1H, d), 7.53 (2H, d), 7.51 (1H, dd), 7.26 (2H, d), 6.81 (1H, d), 2.65 (2H, t), 1.65 (2H, q), 1.34 (8H, m), 0.89 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2921, 1463, 1130, 804, 743
MS *m/z*	292(M^+), 220 207(100%), 178, 165,

Step 2

Preparation of 5-(4-Heptylphenyl)benzo[b]furan-2-boronic acid

The title compound was prepared in a similar manner to that described for the preparation of 4'-pentylbiphenylboronic acid in Example 20(2) using the quantities stated.

5-(4-Heptylphenyl)benzo[b]furan from step 1 (4.0 g, 13.7 mmol), n-butyllithium (2.5M in hexanes, 4.5 ml, 11.3 mmol), trimethyl borate (2.9 g, 27.4 mmol).

A pale-pink solid was obtained.

Yield 4.6 g (99%)

^{1}**H NMR** $CDCl_3/\delta$ 7.82 (1H, d), 7.59 (1H, dd), 7.55 (1H,

	d), 7.53 (2H, d), 7.41 (1H, d), 7.26 (2H, d), 4.94 (2H, s), 2.65 (2H, t), 1.65 (2H, m), 1.33 (8H, m), 0.89 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	3400, 2930, 2850, 1575, 1445, 1330, 1010, 805
MS *m/z*	336(M^+), 292, 207(100%), 178, 107

Step 3

Preparation of 2,5-Bis-(4-heptylphenyl)benzo[b]furan (Compound 66)

Compound 66 was prepared in a similar manner to that described in Example 1(4) using the quantities stated.

5-(4-Heptylphenyl)benzo[b]furan-2-boronic acid (1.5 g, 4.5 mmol), 1-bromo-4-heptylbenzene, (0.8 g, 3.7 mmol), tetrakis(triphenylphosphine)palladium(0) (0.1 g, 0.1 mmol), sodium carbonate (1.0 g, 9.3 mmol).

The product was purified by flash chromatography [silica gel / petroleum fraction (bp 40-60 °C), DCM 9:1], followed by recrystallization (acetonitrile, toluene 5:1)

A colourless crystalline solid was obtained

Yield 0.4 g (26%). Purity (hplc) 98.6%.

^{1}**H NMR** CD_2Cl_2/δ	7.78 (2H, d), 7.75 (1H, dd), 7.54 (2H, d), 7.53 (1H, d), 7.48 (1H, dd), 7.28(2H, d), 7.24 (2H, d), 7.03 (1H, d) 2.53 (4H, t), 1.52 (4H, m), 1.06 (16H, m), 0.57 (6H, t)
IR (KBr) ν_{max}/cm^{-1}	2920, 1465, 1160, 1015, 845, 800
MS *m/z*	466(M^+), (100%), 381, 309, 296, 252

Example 49

Preparation of 5-(4-Heptylphenyl)-2-(4-pentylphenyl)-benzo[b]furan (Compound 67 in Table 1)

The title compound was prepared and purified in a similar manner to that described for the preparation of compound 66 as described in Example 48 using the quantities stated.

5-(4-Heptylphenyl)benzo[b]furan-2-boronic acid (1.5 g, 4.5 mmol), 1-bromo-4-pentylbenzene, (0.8 g, 3.7 mmol), tetrakis(triphenylphosphine)palladium(0) (0.1 g, 0.1 mmol), sodium carbonate (1.0 g, 9.3 mmol).

A white crystalline solid was obtained.

Yield 0.4 g (20%). Purity (hplc) 98.5%.

^{1}**H NMR** CD_2Cl_2/δ	7.80 (2H, d), 7.77 (1H, dd), 7.55 (2H, d), 7.54 (1H, d), 7.50 (1H, dd), 7.29 (2H, d), 7.27 (2H, d), 7.05 (1H, d), 2.67 (2H, t), 2.66 (2H, t), 1.66 (4H, m), 1.33 (12H, m), 0.91 (3H, t), 0.89 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2961, 2857, 1465, 908, 801
MS *m/z*	438(M^+), 381, 353, 296(100%), 283

Example 50

Preparation of 2-(5-Heptylpyrimidin-2-yl)-5-(4-heptylphenyl)benzo[b]furan (Compound 68 in Table 1)

The title compound was prepared and purified in a similar manner to that described in Example 1(4) using the quantities stated.

5-(4-Heptylphenyl)benzo[b]furan-2-boronic acid (1.5 g, 4.5 mmol), 2-chloro-5-heptylpyrimidine (0.8 g, 3.7 mmol), tetrakis(triphenylphosphine)palladium(0) (0.1 g, 0.1 mmol), sodium carbonate (1.0 g, 9.3 mmol).

The product was purified by flash chromatography [silica gel / petroleum fraction (bp 40-60 °C), DCM 1:1], followed by recrystallization (hexane).

Colourless needles-like crystals were obtained.

Yield 0.8 g (46%). Purity (hplc) >99.9%.

^{1}**H NMR** $CDCl_3/\delta$	8.67 (2H, s), 7.85 (1H, d), 7.69 (1H, d), 7.69 (1H, d), 7.60 (1H, dd), 7.55 (2H, d), 7.28 (2H, d), 2.68 (4H, t), 1.67 (4H, m), 1.34 (16H, m), 0.89 (6H, t)
IR (KBr) ν_{max}/cm^{-1}	2923, 2852, 1577, 1542, 1425, 1153, 804, 795

MS *m/z*	468(M^+), 383(100%), 311, 298, 232

Example 51

Preparation of 2-(3,4-Difluorophenyl)-5-(4-heptylphenyl)benzo[b]furan (Compound 69 in Table 1)

The title compound was prepared and purified in a similar manner to that described in Example 1(4) using the quantities stated.

5-(4-Heptylphenyl)benzo[b]furan-2-boronic acid (0.4 g, 1.2 mmol), 1-bromo-3,4-difluorobenzene, (0.2 g, 1.1 mmol), tetrakis(triphenylphosphine)palladium(0) (0.1 g, 0.1 mmol), sodium carbonate (1.0 g, 9.3 mmol).

The product was purified by flash chromatography [silica gel / petroleum fraction (bp 40-60 °C)], followed by recrystallisation (ethanol).

Colourless crystals were obtained.

Yield 0.1 g (12%). Purity (hplc) 98%.

^{1}H NMR CD_2Cl_2/δ	7.79 (1H, dd), 7.72 (1H, ddd), 7.65 (1H, m), 7.58 (2H, d), 7.57 (1H, d), 7.54 (1H, dd), 7.29 (1H, m), 7.28 (1H, m), 7.08 (1H, s), 2.66 (2H, t), 1.65 (2H. qui), 1.32 (8H, m), 0.89 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2925, 2857, 1515, 1468, 1180, 874, 798, 772
MS *m/z*	707(M^+), 319(100%), 305, 289, 159

Example 52

Preparation of 2-(2,3-Difluoro-4-heptylphenyl)-5-(4-heptylphenyl)benzo[b]furan (Compound 70 in Table 1)

Step 1

Preparation of 1-(2,3-Difluorophenyl)heptan-1-ol

n-Butyllithium (2.5M in hexanes, 140.0 ml, 350.0 mmol) was added dropwise to a cooled (-78°C) solution of *O*-difluorobenzene (40.0 g, 350.0 mmol) in dry THF (400 ml) with stirring under nitrogen. Stirring at low temperature was continued (1½ h) and n-heptanal (40.1 g, 333.0 mmol) was added

dropwise. The mixture was allowed to return to room temperature overnight with stirring under nitrogen. 2M hydrochloric acid (225 ml) was added and stirring was continued (1 h). The mixture was then poured into water (400 ml) and ether added (200 ml). The separated aqueous layer was washed with ether (2 x 300 ml). The combined ethereal layers were washed with water and brine and dried ($MgSO_4$), and the solvent removed *in vacuo*. The residue was then distilled.

A pale-yellow oil was obtained.

Yield 63.1 g (83%) bp 140 °C at 0.001 mmHg.

^{1}H NMR CD_2Cl_2/δ	7.24 (1H, m), 7.10 (2H, m), 5.00 (1H, t), 2.25 (1H, s), 1.75 (2H, m), 1.30 (8H, m), 0.88 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	3369, 2931, 1626, 1596, 1484, 1278, 1203, 1061, 786, 726
MS *m/z*	228(M^+), 211, 199, 143(100%), 127

Step 2

Preparation of 1-(2,3-Difluorophenyl)hept-1-ene

Phosphorus pentoxide (94.9 g, 669.0 mmol) was carefully added to a solution of 1-(2,3-Difluorophenyl)heptan-1-ol (61.1 g, 267.0 mmol) from step 1 in pentane (90 ml) and the mixture was stirred overnight with exclusion of moisture. When glc analysis revealed a complete reaction, the mixture was poured into ice/water (300 ml) and ether added (200 ml). The separated aqueous layer was washed with ether (2 x 300 ml). The combined organic layers were washed with water and brine and dried ($MgSO_4$), and the solvent removed *in vacuo*. The residue was then distilled.

A colourless oil was obtained.

Yield 30.9 g (55%) bp 95 °C at 0.05 mmHg.

^{1}H NMR $CDCl_3/\delta$	7.16 (1H, m), 6.97 (2H, m), 6.51 (1H, d), 6.34 (1H, dt) 2.23 (2H, q), 1.48 (2H, qui), 1.34 (4H, m), 0.91 (3H, t)

IR (KBr) ν_{max}/cm^{-1} 2929, 1621, 1589, 1482, 1205, 972, 773, 712

MS *m/z* 210(M^{+}), 167, 153, 140(100%), 127

Step 3

Preparation of 1,2-Difluoro-3-heptylbenzene

A mixture of the product of step 2 (30.5 g, 145 mmol) and palladium-on-charcoal (10% w/w, 1.0 g, 0.9 mmol) in ethanol (400 ml) was stirred in an atmosphere of hydrogen (glc analysis revealed a complete reaction). The mixture was then filtered through a pad of 'Hyflo Supercel' and the solvent was removed *in vacuo*. The product was purified by distillation.
A pale yellow liquid was obtained.

Yield 26.4 g (86%) bp 95 °C at 0.003 mmHg.

^{1}**H NMR** $CDCl_3/\delta$ 6.95 (3H, m), 2.65 (2H, t), 1.60 (2H, qui), 1.31 (8H, m), 0.88 (3H, t)

IR (KBr) ν_{max}/cm^{-1} 2929, 2858, 1628, 1595, 1490, 1209, 822, 780, 725

MS *m/z* 212(M^{+}), 141, 127(100%), 114, 83

Step 4

Preparation of 2,3-Difluoro-1-iodo-4-heptylbenzene

n-Butyllithium (2.5M in hexanes, 14.4 ml, 36.0 mmol) was added dropwise to a cooled (-78°C) solution of the product of step 3 (7.0 g, 33.0 mmol) in dry THF (100 ml) with stirring under nitrogen. Stirring at low temperature was continued (1 h) and iodine (8.4 g, 33.0 mmol) in dry THF (100 ml) was added dropwise, maintaining low temperature. The mixture was allowed to return to room temperature overnight with stirring under nitrogen. It was then poured into water (50 ml) and ether added (50 ml). The separated aqueous layer was washed with ether (2 x 50 ml) and the combined organic layers were washed with saturated aqueous sodium sulphite, water and brine, and dried ($MgSO_4$), and the solvent removed *in vacuo*.
The product was purified by distillation.

A pale-pink liquid was obtained.

Yield 5.0 g (45%) bp 125 °C at 0.005 mmHg.

^{1}**H NMR** $CDCl_3/\delta$	7.37 (1H, ddd), 6.73 (1H, ddd), 2.63 (2H, dt), 1.58 (2H, t), 1.29 (8H, m), 0.88 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2927, 2856, 1457, 1285, 866, 806, 724, 612, 546
MS *m/z*	338(M^+), 254, 139, 127(100%), 107

Step 5

Preparation of 2-(2,3-Difluoro-4-heptylphenyl)-5-(4-heptylphenyl)benzo[b]furan

Compound 70 in Table 1 was prepared in a similar manner to that described for the preparation of compound 66 in Example 48(3) using the quantities stated. 5-(4-Heptylphenyl)benzo[b]furan-2-boronic acid (0.6 g, 1.8 mmol), the product of step 4 (0.6 g, 1.6 mmol), tetrakis(triphenylphosphine)palladium(0) (0.1 g, 0.1 mmol), sodium carbonate (0.4 g, 4.0 mmol). The product was purified by flash chromatography [silica gel / petroleum fraction (bp 40-60 °C)], followed by recrystallisation (hexane).

A white crystalline solid was obtained.

Yield 0.3 g (37%). Purity (hplc) >99%.

^{1}**H NMR** CD_2Cl_2/δ	7.81 (1H, dd), 7.69 (1H, ddd), 7.57 (2H, m), 7.56 (2H, d), 7.28 (2H, d), 7.25 (1H, dd), 7.10 (1H, ddd), 2.72 (2H, t), 2.66 (2H, t), 1.65 (4H, qui), 1.33 (16H, m), 0.89 (6H, t)
IR (KBr) ν_{max}/cm^{-1}	2927, 2856, 1498, 1123, 965, 878, 809, 726
MS *m/z*	502(M^+)(100%), 417, 332, 166, 58

Example 53

Preparation of 2-(Hept-1-ynyl)-5-(4-heptylphenyl)benzo[b]furan (Compound 17 in Table 1)

Step 1

Preparation of 2-Iodo-5-(4-heptylphenyl)benzo[b]furan

n-Butyllithium (2.5M in hexanes, 3.8 ml, 9.4 mmol) was added dropwise to a cooled (-10°C) solution of 5-(4-Heptylphenyl)benzo[b]furan_(2.5 g, 8.6 mmol) (prepared as described in Example 48(1) in dry THF (100 ml) with stirring under nitrogen. Stirring at low temperature was continued (2 h), and iodine (4.3 g, 17.2 mmol) in dry ether (30 ml) was added dropwise. After stirring at low temperature for a further 30 min the mixture was allowed to return to room temperature. It was then poured into water (50 ml) and ether added (50 ml). The separated aqueous layer was washed with ether (2 x 50 ml). The combined ethereal layers were washed with saturated aqueous sodium sulphite, water and brine, and dried ($MgSO_4$). The solvent was removed *in vacuo*. The product was purified by recrystallization (hexane).

Colourless plate-like crystals were obtained.

Yield 2.5 g (70%), mp 94-95 °C

^{1}H NMR CD_2Cl_2/δ	7.71 (1H, d), 7.52 (1H, d), 7.51 (2H, d), 7.46 (1H, dd), 7.04 (1H, d), 2.65 (2H, t), 1.64 (2H, qui), 1.31 (8H, m), 0.89 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2922, 2849, 1524, 1446, 1232, 1147, 1048, 918, 897, 884, 668
MS *m/z*	418(M^+), 333, 207, 178, 43(100%),

Step 2

Preparation of 2-(Hept-1-ynyl)-5-(4-heptylphenyl)benzo[b]furan

n-Butyllithium (2.5M in hexanes, 2.8 ml, 6.9 mmol) was added dropwise to a cooled (-40°C) solution of hept-1-yne (0.6 g, 6.3 mmol) in dry THF (17 ml) with stirring under nitrogen. Stirring at low temperature was continued (20 min), and a

solution of anhydrous zinc chloride (1.1 g, 8.0 mmol) in dry THF (30 ml) was added dropwise, maintaining low temperature. Stirring under nitrogen was continued (4 h) and the mixture was allowed to return to room temperature. The product of step 1 (2.4 g, 5.7 mmol) and tetrakis(triphenylphosphine)palladium(0) (0.2 g, 0.2 mmol) were added, and the mixture was heated (70 °C) with stirring under nitrogen (12 h). When glc/tlc analysis revealed no further reaction the mixture was poured into water (50 ml) and ether added (50 ml). The separated aqueous layer was washed with ether (2 x 50 ml). The combined organic layers were washed with water and brine and dried ($MgSO_4$), and the solvent removed *in vacuo*. The product was purified by flash chromatography [silica gel / petroleum fraction (bp 40-60 °C)]. A yellow crystalline solid was obtained.

Yield 0.9 g (42%). Purity (hplc) 99.5%.

^{1}**H NMR** CD_2Cl_2/δ	7.72 (1H, d), 7.54 (1H, dd), 7.53 (2H, d), 7.47 (1H, d), 7.27 (2H, d), 6.88 (1H, s), 2.65 (2H, t), 2.51 (2H, t), 1.67 (4H, m), 1.40 (12H, m), 0.95 (3H, t), 0.90 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2929, 2859, 2210, 1570, 1265, 992, 886, 842, 749, 727
MS *m/z*	386(M^+), 371, 301(100%), 244, 207

Example 54

Preparation of 2-(4-heptylphenyl)-5-(hept-1-ynylphenyl)benzo[b]furan (Compound 71 in Table 1)

Step 1

Preparation of 5-(Hept-1-ynylphenyl)benzo[b]furan)

The title compound was prepared and purified in a similar manner to that described for the preparation of compound 17 in Example 53 using the quantities stated. n-Butyllithium (2.5M in hexanes, 4.8 ml, 12.0 mmol), hept-1-yne (1.1 g, 11.0 mmol), zinc chloride (1.9 g, 14.0 mmol), 4-bromobenzofuran (2.0 g, 10.0 mmol).

A yellow liquid was obtained.

Yield 1.2 g (57%)

^{1}**H NMR** CD_2Cl_2/δ	7.65 (2H, d), 7.42 (1H, d), 7.33 (1H, dd), 6.76 (1H, dd), 2.42 (2H, t), 1.63 (2H, qui), 1.41 (4H, m), 0.94 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2936, 2866, 1465, 1131, 1032, 883, 768, 735
MS *m/z*	212(M^{+}), 197, 183, 169, 154(100%)

Step 2

Preparation of 5-(Hept-1-ynylphenyl)benzo[b]furan-2-boronic acid

The title compound was prepared in a similar manner to that described in Example 20(2) using the quantities stated. 5-(Hept-1-ynylphenyl)benzo[b]furan) from step 1 (1.0 g, 5.2 mmol), n-butyllithium (2.5M in hexanes, 2.3 ml, 5.7 mmol), trimethyl borate (1.2 g, 11.4 mmol).

An orange solid was obtained.

Yield 1.0 g (83%)

MS *m/z* 232(M^{+}), 212, 183, 169, 155(100%)

Step 3

Preparation of 2-(4-heptylphenyl)-5-(hept-1-ynylphenyl)benzo[b]furan (Compound 71 in Table 1)

The title compound was prepared and purified in a similar manner to that described for the preparation of compound 70 in Example 52 using the quantities stated. 5-(Hept-1-ynylphenyl)benzo[b]furan-2-boronic acid from step 2 (1.0 g, 4.3 mmol), 1-bromo-4-heptylbenzene (Example 1(1)) (1.1 g, 4.3 mmol), tetrakis(triphenylphosphine)palladium(0) (0.2 g, 0.2 mmol), sodium carbonate (1.1 g, 11.0 mmol).

Yield 0.3 g (18%). Purity (hplc) 85.1%.

^{1}**H NMR** CD_2Cl_2/δ	7.76 (2H, d), 7.61 (1H, d), 7.42 (1H, d), 7.29 (1H, dd), 7.28 (2H, d), 6.96 (1H, s), 2.65 (2H, t), 2.42 (2H, t), 1.63 (4H,

	qui), 1.35 (12H, m), 0.94 (3H, t), 0.89 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2935, 2859, 1906, 1700, 1653, 1636, 1467, 1274, 878, 798
MS *m/z*	386 (M^+)(100%), 343, 301, 244, 215

Example 55

Preparation of 2-(4-Heptylphenyl)-5-(4-pentylphenyl)benzo[b]furan (Compound 72 in Table 1)

Step 1

Preparation of 1-Heptyl-4-iodobenzene

The title compound was prepared and purified in a similar manner to that described in Example 1(1) using the quantities stated.

Iodobenzene (20.4 g, 100 mmol), n-heptanoyl chloride (17.8 g, 120 mmol), aluminium chloride (14.7 g, 110 mmol), poly(methylhydrosiloxane) (16.1 g 267 mmol).

The compound was prepared and stored under exclusion of light. A pale-yellow liquid was obtained.

Yield 12.2 g (40%) bp 120 °C at 0.005 mmHg (lit.[2] 165°C at 10 mmHg).

^{1}**H NMR** CD_2Cl_2/δ	7.60 (2H, d), 6.96 (2H, d), 2.51 (2H, t), 1.60 (2H, m), 1.35-1.25 (8H, m), 0.90 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2926, 2854, 1466, 1062, 995, 794
MS *m/z*	302(M^+)(100%), 259, 231, 217, 127

Step 2

Preparation of 2-(4-Heptylphenyl)-5-bromobenzo[b]furan

The title compound was prepared in a similar manner to that described in Example 1(4) using the quantities stated.

1-Heptyl-4-iodobenzene from step 1 (2.1 g, 7.0 mmol), 4-bromobenzo[b]furan-2-boronic acid (2.0 g, 8.0 mmol), sodium carbonate (1.9 g, 18.0 mmol), tetrakis(triphenylphosphine)palladium(0) (0.2 g, 0.2 mmol)

The product was purified by flash chromatography [silica gel / petroleum fraction (bp 40-60 °C)], followed by recrystallisation (hexane).

A white solid was obtained.

Yield 0.5 g (20%), mp 144-149 °C

^{1}H NMR CD_2Cl_2/δ	7.68 (2H, d), 7.62 (1H, d), 7.32 (1H, d), 7.28 (1H, dd), 7.20 (2H, d), 6.87 (1H, s), 2.57 (2H, t), 1.56 (2H, t), 1.23 (8H, m), 0.80 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2930, 2858, 1609, 1582, 1035, 922, 895, 670, 505
MS *m/z*	372,370(M$^+$), 285(100%), 205, 176, 152

Step 3

Preparation of 2-(4-Heptylphenyl)-5-(4-pentylphenyl)benzo[b]furan (Compound 72 in Table 1)

The title compound was prepared in a similar manner to that described in Example 1(4) using the quantities stated.

2-(4-Heptylphenyl)-5-bromobenzo[b]furan (0.4 g, 1.1 mmol), 4-pentylbenzeneboronic acid (0.3 g, 1.3 mmol), sodium carbonate (0.3 g, 2.8 mmol), tetrakis(triphenylphosphine)palladium(0) (0.1 g, 0.1 mmol)

The product was purified by flash chromatography [silica gel / petroleum fraction (bp 40-60 °C)], followed by recrystallisation (hexane).

A white crystalline solid was obtained.

Yield 0.4 g (83%). Purity (hplc) 98.4%.

^{1}H NMR CD_2Cl_2/δ	7.79 (2H, d), 7.77 (1H, d), 7.56 (1H, d), 7.55 (2H, d), 7.50 (1H, dd), 7.30 (2H, d), 7.28 (2H, d), 7.05 (1H, s), 2.66 (4H, t) 1.66 (4H, m), 1.33 (12H, m), 0.92 (3H, t), 0.89 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2963, 2928, 2858, 1589, 1121, 1034, 884, 799
MS *m/z*	438(M$^+$), 381, 353, 296, 43(100%)

Example 56

Preparation of Compound 73 in Table 1

Step 1

Preparation of 1-Heptyl-2,3-difluorobenzene-4-boronic acid

The title compound was prepared in a similar manner to that described for the preparation of 4'-pentylbiphenylboronic acid in Example 20(2) using the quantities stated.

1,2-Difluoro-3-heptylbenzene prepared as described in Example 52(3) (19.2 g, 90.0 mmol), n-butyllithium (2.5M in hexanes, 39.8 ml, 99.0 mmol), trimethyl borate (18.7 g, 180.0 mmol).

A white solid was obtained.

Yield 19.9 g (87%)

^{1}H NMR DMSO-d^6/δ	7.11 (1H, m), 7.10 (1H, m), 2.62 (2H, dt), 1.54 (2H, qui), 1.24 (8H, m), 0.84 (3H, t) (acidic proton was not shown)
IR (KBr) ν_{max}/cm^{-1}	3661, 3342, 2939, 2849, 1628, 1425, 1190, 929, 902, 835, 723
MS *m/z*	212 (M^+-B$(OH)_2$+H), 169, 140, 128(100%), 101

Step 2

Preparation of 5-(2,3-Difluoro-4-heptylphenyl)benzo[b]furan

The title compound was prepared in a similar manner to that described in Example 1(4) using the quantities stated.

4-bromobenzofuran (1.8 g, 9.0 mmol), 1-Heptyl-2,3-difluorobenzene-4-boronic acid from step 1 (2.8 g, 10.8 mmol), sodium carbonate (2.4 g, 23.0 mmol), tetrakis(triphenylphosphine)palladium(0) (0.3 g, 0.3 mmol)

The product was purified by flash chromatography [silica gel / petroleum fraction (bp 40-60 °C)], followed by recrystallisation (hexane).

A pale-yellow liquid was obtained.

Yield 1.4 g (47%)

^{1}H NMR CD_2Cl_2/δ	7.77 (1H, s), 7.70 (1H, d), 7.58 (1H, dd), 7.46 (1H, ddd), 7.16 (1H, ddd), 7.04 (1H, ddd), 6.85 (1H, d), 2.71 (2H, t),

	1.66 (2H, qui), 1.38 (8H, m), 0.91 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2933, 2861, 1468, 1113, 890, 808, 772, 739
MS *m/z*	328(M^+), 243, 231, 194, 43(100%)

Step 3

Preparation of 5-(2,3-Difluoro-4-heptylphenyl)benzo[b]furan-2-boronic acid)

The title compound was prepared in a similar manner to that described for the preparation of 4′-pentylbiphenylboronic acid in Example 20(2) using the quantities stated.

The product of step 2 (1.2 g, 3.7 mmol), n-butyllithium (2.5M in hexanes, 1.6 ml, 4.0 mmol), trimethyl borate (0.8 g, 7.4 mmol).

A white solid was obtained.

Yield 1.1 g (80%)

MS *m/z* 328(M^+-B(OH)$_2$), 256, 243(100%), 201, 175

Step 4

Preparation of 5-(2,3-Difluoro-4-heptylphenyl)-2-(4-heptylphenyl)-benzo[b]furan (Compound 73 in Table 1)

The title compound was prepared in a similar manner to that described for the preparation of in Example 1(4) using the quantities stated.

1-bromo-4-heptylbenzene (0.8 g, 3.0 mmol), 5-(2,3-Difluoro-4-heptylphenyl)benzo[b]furan-2-boronic acid) from step 3 (1.1 g, 3.0 mmol), sodium carbonate (0.8 g, 8.0 mmol), tetrakis(triphenylphosphine)palladium(0) (0.1 g, 0.1 mmol).

A white, fibrous, crystalline solid was obtained.

Yield 0.4 g (27%). Purity (hplc) 98.4%.

^{1}**H NMR** CD_2Cl_2/δ	7.80 (2H, d), 7.73 (1H, m), 7.58 (1H, d), 7.43 (1H, ddd), 7.30 (2H, d), 7.18 (1H, m), 7.05 (1H, d), 7.04 (1H, m), 2.71 (2H,

	t), 2.66 (2H, t), 1.66 (4H, m), 1.33 (16H, m), 0.90 (3H, t), 0.89 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2936, 2856, 1509, 1121, 1033, 916, 802, 754
MS *m/z*	502(M^+), 417, 332, 224, 91(100%)

Example 57

Preparation of Compound 74 in Table 1

Step 1

Preparation of 5-(5-Heptylpyrimidin-2-yl)benzo[b]furan

The title compound was prepared and purified in a similar manner to that described for the preparation of compound 68 in Table 1 using the quantities stated.

Benzo[b]furan-5-boronic acid (Example 22(1)) (0.7 g, 4.2 mmol), 2-chloro-5-heptylpyrimidine (0.8 g, 3.7 mmol) tetrakis(triphenylphosphine)palladium(0) (0.1 g, 0.1 mmol), sodium carbonate (0.9 g, 8.8 mmol).

A pale-yellow, waxy solid was obtained

Yield 0.9 g (83%)

^{1}**H NMR** $CDCl_3/\delta$	8.69 (1H, d), 8.62 (2H, s), 8.42 (1H, dd), 7.65 (1H, d), 7.58 (1H, d), 6.84 (1H, dd), 2.61 (2H, t), 1.65 (2H, qui), 1.31 (8H, m), 0.87 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2928, 2856, 1588, 1547, 1130, 1029, 796, 768, 737
MS *m/z*	294(M^+), 265, 251, 223, 209(100%)

Step 2

Preparation of 5-(5-Heptylpyrimidin-2-yl)benzo[b]furan-2-boronic acid

n-Butyllithium (2.5M in hexanes, 2.0 ml, 5.1 mmol) was added dropwise to a cooled (-70 °C) solution of dry diisopropylamine (2.0 g, 20.0 mmol) in dry THF (15 ml) with stirring under nitrogen. Stirring was continued (10 min), and 5-(5-Heptylpyrimidin-2-yl)benzo[b]furan from step 1(1.5 g, 5.1 mmol)

in dry THF (7 ml) was added dropwise at -70°C. After stirring under nitrogen (1 h) trimethyl borate (1.0 g, 10.0 mmol) was added dropwise at low temperature. The system was allowed to return to room temperature overnight whilst stirring under nitrogen. Hydrochloric acid (5M, 4.0 ml) was added with stirring. The mixture was then poured into water (100 ml) and ether added (50 ml). The separated aqueous layer was washed with ether (3 x 50 ml). The combined organic layers were washed with water and brine, and dried ($MgSO_4$), and the solvent removed *in vacuo*. The residue was adsorbed onto silica and washed with petroleum fraction (bp 40-60 °C). The adsorbate was then washed with THF, and the solvent removed *in vacuo*. An orange solid was obtained.

Yield 1.4 g (78%)

MS *m/z* 294(M^+-B(OH_2)), 223, 209(100%), 195, 181

Step 3

Preparation of 2-(2,3-Difluoro-4-heptyl)-5-(5-heptylpyrimidin-2-yl)benzo[b]furan (Compound 74)

The title compound was prepared in a similar manner to that described for the preparation of compound 68 in Table 1 using the quantities stated.

5-(5-Heptylpyrimidin-2-yl)benzo[b]furan-2-boronic acid from step 2 (1.3 g, 3.8 mmol), 2,3-Difluoro-1-iodo-4-heptylbenzene (Example 52 (4) (1.5 g, 4.6 mmol), tetrakis(triphenylphosphine)palladium(0) (0.2 g, 0.2 mmol), sodium carbonate (1.2 g, 12.0 mmol). The product was purified by flash chromatography [silica gel / petroleum fraction (bp 40-60 °C), DCM 7:3], followed by recrystallisation (ethanol, DCM 9:1), and finally, by preparative hplc (acetonitrile, chloroform 4:1).

Colourless needle-like crystals were obtained.

Yield 0.4 g (17%). Purity (hplc) >99.9%.

^{1}**H NMR** CD_2Cl_2/δ 8.71 (1H, d), 8.62 (2H, s), 8.44 (1H, dd), 7.68 (1H, ddd), 7.59 (1H, d), 7.27 (1H, dd), 7.09 (1H, ddd), 2.70 (2H, t),

	2.62 (2H, t), 1.66 (2H, qui), 1.64 (2H, t), 1.36-1.24 (16H, m), 0.87 (6H, t)
IR (KBr) ν_{max}/cm^{-1}	2932, 2859, 1586, 1549, 1328, 1117, 964, 875, 797
MS *m/z*	504(M^+)(100%), 462, 433, 419, 321

Example 58

Preparation of Compound 75 in Table 1

Step 1

Preparation of 1,2-Difluorobenzene-3-boronic acid

The title compound was prepared in a similar manner to that described in Example 20(2) using the quantities stated. O-difluorobenzene (65.8 g, 577.0 mmol), n-butyllithium (2.5M in hexanes, 231.0 ml, 577.0 mmol), trimethyl borate (71.9 g, 692.0 mmol).

The reaction mixture was poured into water (200 ml) and ether added (200 ml). The separated aqueous phase was washed with ether (3 x 200 ml). The product was extracted from the combined ethereal phases as the potassium salt by washing with potassium hydroxide (2M, 290 ml). The basic solution was then washed with ether, and the product released by acidification to pH3 by adding hydrochloric acid (conc.) to the aqueous solution. The product was then extracted with ether (3 x 200 ml). The combined organic layers were washed with water and brine, dried ($MgSO_4$), and the solvent removed *in vacuo*.

A white solid was obtained. Yield 47.1 g (52%)

MS *m/z* 420 ($3M^+$-$3H_2O$)(100%), 280, 140, 94, 75

Step 2

Preparation of 2,3-Difluorophenol

Hydrogen peroxide (100 vol, 197.0 ml, 1.74 mol) was added slowly to a stirred solution of 1,2-difluorobenzene-3-boronic acid (458. g, 290.0 mmol) in dry diethyl ether (300 ml) and the mixture was refluxed (2 h). After allowing to cool, the mixture was washed with ether (3 x 250 ml). The combined

ethereal layers were washed with saturated aqueous sodium thiosulphate, water and brine and dried ($MgSO_4$), and the solvent removed *in vacuo*. The product was purified by distillation.

A colourless liquid was obtained, which solidified on cooling.

Yield 24.2 g (64%) bp 150 °C at 760 mmHg.

^{1}**H NMR** $CDCl_3/\delta$	6.95 (1H, m), 6.75 (2H, m), 4.95 (1H, s)
IR (KBr) ν_{max}/cm^{-1}	3187, 2986, 1623, 1534, 1196, 1023, 889, 773, 701
MS *m/z*	130(M^+)(100%), 101, 82, 71, 56

Preparation of 4-Bromo-2,3-difluorophenol

Bromine (29.1 g, 182.0 mmol) in glacial acetic acid (45 ml) was carefully added dropwise, maintaining low temperature, to a vigorously stirred, cooled (10 °C) solution of 2,3-difluorophenol (21.4 g, 165.0 mmol) in glacial acetic acid / chloroform 4:1 (55 ml) Stirring was continued (15 min) and the mixture was poured into water (200 ml) and DCM added (100 ml). The separated aqueous layer was washed with DCM (3 x 100 ml), and the combined organic layers were washed with saturated aqueous sodium bicarbonate, water and brine and dried ($MgSO_4$). The solvent was then removed *in vacuo*. Hexane (100 ml) was added to the residue and the mixture was heated until homogeneous. It was then cooled (8 °C) and the solvent was removed by filtration. The product was then distilled.

A colourless liquid was obtained.

Yield 26.7 g (77%) bp 135-160 °C at 20 mmHg.

^{1}**H NMR** $CDCl_3/\delta$	7.22 (1H, m), 6.71 (1H, m), 5.57 (1H, s)
IR (KBr) ν_{max}/cm^{-1}	3395, 2970, 1622, 1187, 1032, 876, 798, 630, 535
MS *m/z*	210,208(M^+), 179, 128, 101, 81(100%)

NMR revealed approximately 33% impurity, consisting of starting material and dibromination product. Further purification was carried out after the next synthetic step.

Step 4

Preparation of 2-(4-Bromo-2,3-difluorophenoxy)acetaldehyde dimethyl acetal

The title compound was prepared in a similar manner to that described in Example 9(1) using the quantities stated.

The product of step 3 (28.6 g, 137.0 mmol), bromoacetaldehyde dimethyl acetal (25.5 g, 151.0 mmol), potassium carbonate (37.9 g, 274.0 mmol) and potassium iodide (1.1 g, 7.0 mmol).

The crude product was purified by flash chromatography [neutral alumina / petroleum fraction (bp 40-60 °C), DCM 10:3], followed by distillation.

A colourless liquid was obtained.

Yield 17.4 g (46%) bp 127 °C at 0.05 mmHg.

^{1}H NMR $CDCl_3/\delta$	7.21 (1H, m), 6.70 (1H, m), 4.71 (1H, t), 4.05 (2H, d), 3.47 (6H, s)
IR (KBr) ν_{max}/cm^{-1}	2945, 2842, 1619, 1504, 1140, 880, 795, 593
MS *m/z*	298,296(M^+), 265, 235, 207, 75(100%)

Step 5

Preparation of 5-Bromo-6,7-difluorobenzo[b]furan

The title compound was prepared and purified in a similar manner to that described for the preparation of 5-bromobenzo[b]furan in Example 9(2) using the quantities stated.

The product of step 4 (9.7 g, 33.0 mmol), polyphosphoric acid (13.9 g).

The product was further purified by recrystallization (ethanol).

White needle-like crystals were obtained.

Yield 1.9 g (25%), mp 96.5-98.0 °C

^1H **NMR** CD_2Cl_2/δ	7.73 (1H, d), 7.58 (1H, dd), 6.80 (1H, dd)
IR (KBr) ν_{max}/cm^{-1}	1603, 1485, 1125, 1084, 876, 814, 765, 730, 640, 531
MS *m/z*	234,232 (M^+), 153, 125, 105(100%), 77

Step 6

Preparation of 5-Bromo-6,7-difluorobenzo[b]furan-2-boronic acid

The title compound was prepared and purified in a similar manner to that described for the preparation of 5-(5-Heptylpyrimidin-2-yl)benzo[b]furan-2-boronic acid (Example 57(2) using the quantities stated.

n-Butyllithium (2.5M in hexanes, 5.2 ml, 13.0 mmol) dry diisopropylamine (1.3 g, 13.0 mmol), the product of step 5 (3.0 g, 13.0 mmol), trimethyl borate (2.7 g, 26.0 mmol), hydrochloric acid (5M, 5.2 ml).

A cream-coloured solid was obtained.

Yield 3.1 g (86%)

MS *m/z* 777,775($3M^+-3H_2O$), 705(100%), 626, 231, 124

Step 7

Preparation of 5-Bromo-6,7-difluoro-2-(4-pentylphenyl)benzo[b]furan

The title compound was prepared and purified in a similar manner to that described for the preparation of 5-(4-pentylphenyl)benzo[b]furan (Example 24 (1) using the quantities stated.

4-Iodo-4-pentylbenzene (Example 22(2) (1.8 g, 6.7 mmol), the product of step 6 (1.6 g, 5.6 mmol), sodium carbonate (1.8 g, 17.0 mmol), tetrakis(triphenylphosphine)palladium(0) (0.2 g, 0.2 mmol)

A white, crystalline solid was obtained.

Yield 1.2 g (57%), mp 62-64 °C

^{1}**H NMR** CD_2Cl_2/δ	7.76 (2H, d), 7.54 (1H, dd), 7.30 (2H, d), 6.96 (1H, d), 2.66 (2H, t), 1.65 (2H, qui), 1.34 (4H, m), 0.90 (3H, t).
IR (KBr) ν_{max}/cm^{-1}	2932, 2866, 1605, 1442, 1043, 909, 795, 548
MS *m/z*	380,378(M^+), 321(100%), 241, 213, 193

Step 8

Preparation of 6,7-Difluoro-5-(4-heptylphenyl)-2-(4-pentylphenyl)benzo[b]furan (Compound 75 in Table 1)

The title compound was prepared in a similar manner to that described in Example 1(4) using the quantities stated. Product of step 7 (1.2 g, 3.2 mmol), 4-heptylbenzeneboronic acid (0.9 g, 3.8 mmol), sodium carbonate (0.9 g, 8.0 mmol), tetrakis(triphenylphosphine)palladium(0) (0.1 g, 0.1 mmol) The product was purified by flash chromatography [silica gel / petroleum fraction (bp 40-60 °C)], followed by recrystallisation (ethanol). It was then dissolved in carbon tetrachloride/chloroform 19:1. The solution was triturated with methanol, the precipitate filtered, and washed with ethanol.

Colourless, needle-like crystals were obtained.

Yield 0.4 g (23%). Purity (hplc) 99%.

^{1}**H NMR** CD_2Cl_2/δ	7.79 (2H, d), 7.47 (2H, d), 7.34 (1H, dd), 7.31 (2H, d), 7.30 (2H, d), 7.02 (1H, d), 2.67 (2H, t), 2.66 (2H, t), 1.66 (4H, qui), 1.37-1.26 (12H, m), 0.91 (3H, t), 0.89 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2960, 2857, 1613, 1513, 1160, 1038, 910, 838, 807, 661
MS *m/z*	474(M^+)(100%), 417, 389, 331, 232

Example 59

Preparation of 6,7-Difluoro-2-(2,3-difluoro-4-heptylphenyl)-5-(4-heptylphenyl)benzo[b]furan (Compound 76 in Table 1)

Step 1

Preparation of 5-Bromo-6,7-difluoro-2-(2,3-difluoro-4-heptylphenyl)benzo[b]furan)

The title compound was prepared and purified in a similar manner to that described in Example 24(1) using the quantities stated.

2,3-Difluoro-1-iodo-4-heptylbenzene (Example 52 (4) (2.3 g, 6.7 mmol), 5-Bromo-6,7-difluorobenzo[b]furan-2-boronic acid (Example 58(6))(1.6 g, 5.6 mmol), sodium carbonate (1.8 g, 17.0 mmol), tetrakis(triphenylphosphine)palladium(0) (0.2 g, 0.2 mmol)

A white, crystalline solid was obtained.

Yield 0.6 g (24%), mp 62-65 °C

^{1}**H NMR** CD_2Cl_2/δ	7.69 (1H, ddd), 7.60 (1H, dd), 7.18 (1H, dd), 7.12 (1H, ddd), 2.72 (2H, dt), 1.65 (2H, qui), 1.31 (8H, m), 0.89 (3H, t).
IR (KBr) ν_{max}/cm^{-1}	2932, 2856, 1605, 1476, 1210, 1031, 932, 869, 731, 606
MS *m/z*	444,442(M^+)(100%), 357, 277, 249, 230

Step 2

Preparation of 6,7-Difluoro-2-(2,3-difluoro-4-heptylphenyl)-5-(4-heptylphenyl)benzo[b]furan (Compound 76 in Table 1)

The title compound was prepared in a similar manner to that describedin Example 24(1) using the quantities stated.

The product of step 1 (0.6 g, 1.2 mmol), 4-heptylbenzeneboronic acid (0.3 g, 1.5 mmol), sodium carbonate (0.3 g, 3.0 mmol), tetrakis(triphenylphosphine)palladium(0) (0.1 g, 0.1 mmol)

The product was purified by flash chromatography [silica gel / petroleum fraction (bp 40-60 °C)], followed by recrystallisation (ethanol).

Colourless, plate-like crystals were obtained.

Yield 0.1 g (17%). Purity (hplc) >99%.

^{1}H NMR CD_2Cl_2/δ	7.72 (1H, ddd), 7.47 (2H, dd), 7.40 (1H, dd), 7.30 (2H, d), 7.25 (1H, dd), 7.12 (1H, ddd), 2.72 (2H, t), 2.67 (2H, t), 1.39-1.62 (4H, m), 1.37-1.28 (16H, m), 0.90 (3H, t), 0.89 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2928, 2857, 1616, 1475, 1164, 1093, 932, 879, 809, 719
MS *m/z*	538(M^+)(100%), 467, 453, 368, 184

Example 60

Preparation of Compound 77 in Table 1

Step 1

Preparation of 5-(2,3-Difluoro-4-heptyl)-6,7-difluorobenzo[b]furan

The title compound was prepared and purified in a similar manner to that described in Example 24(1) using the quantities stated.

5-Bromo-6,7-difluorobenzo[b]furan (1.1 g, 4.7 mmol), 1-heptyl-2,3-difluorobenzene-4-boronic acid (1.4 g, 5.6 mmol), sodium carbonate (1.3 g, 12.0 mmol), tetrakis(triphenylphosphine)palladium(0) (0.2 g, 0.2 mmol) After refluxing (1 day) tlc and glc analysis revealed some starting material still remained, so compound 161 (0.6 g, 2.3 mmol) and catalyst (0.1 g, 0.1 mmol) were added.

A white, crystalline solid was obtained.

Yield 0.8 g (47%), mp 57-59.5 °C

^{1}H NMR CD_2Cl_2/δ	7.75 (1H, d), 7.35 (1H, ddd), 7.08 (2H, m), 6.87 (1H, dd), 2.73 (2H, dt), 1.66 (2H, qui), 1.34 (8H, m), 0.90 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2921, 2859, 1618, 1512, 1121, 1046, 963, 807, 738, 671
MS *m/z*	364(M^+), 335, 279(100%), 250, 201

Step 2

Preparation of 5-(2,3-Difluoro-4-heptyl)-6,7-difluorobenzo[b]furan-2-boronic acid

The title compound was prepared and purified in a similar manner to that described for the preparation of 4'-pentylphenylboronic acid (Example 20(2)) using the quantities stated.

Product of step 1 (0.7 g, 1.9 mmol), n-butyllithium (2.5M in hexanes, 0.9 ml, 2.3 mmol), trimethyl borate (0.4 g, 3.8 mmol). A white solid was obtained.

Yield 0.8 g (quant).

MS *m/z* 364(M^+-$B(OH)_2$), 292, 279(100%), 250, 121

Step 3

Preparation of 2-(4-Heptylphenyl)-5-(2,3-difluoro-4-heptyl)-6,7-difluorobenzo[b]furan (Compound 77)

The title compound was prepared and purified in a similar manner to that described in Example 24(1) using the quantities stated.

1-Heptyl-4-iodobenzene (0.7 g, 2.4 mmol), the product of step 2 (0.8 g, 2.0 mmol), sodium carbonate (0.6 g, 5.7 mmol), tetrakis(triphenylphosphine)palladium(0) (0.1 g, 0.1 mmol) Final purification was by preparative hplc (acetonitrile/chloroform 4:1).

A white, crystalline solid was obtained.

Yield 0.1 g (5%). Purity (hplc) >99.9%.

^{1}H NMR CD_2Cl_2/δ	7.80 (2H, d), 7.32 (1H, m), 7.31 (2H, d), 7.13-7.07 (1H, m), 7.12-7.06 (1H, m), 7.04 (1H, d), 2.73 (2H, dt), 2.67 (2H, t), 1.69 (2H, qui), 1.67 (2H, qui), 1.38-1.26 (16H, m), 0.90 (3H, t), 0.89 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2929, 2859, 1618, 1279, 1053, 969, 908, 835, 811
MS *m/z*	538(M^+)(100%), 453, 416, 368, 290

Example 61

Preparation of Compound 78 in Table 1

Step 1

Preparation of 2,3-Difluoro-4-heptylphenol

The title compound was prepared and purified in a similar manner to that described for in Example 58(2) using the quantities stated.

Hydrogen peroxide (100 vol, 27.0 ml, 238.0 mmol), 1-heptyl-2,3-difluorobenzene-4-boronic acid (10.0 g, 39.0 mmol).

A colourless liquid was obtained.

Yield 5.9 g (66%), bp 205 °C at 20 mmHg.

^{1}H NMR CD_2Cl_2/δ	6.82 (1H, ddd), 6.69 (1H, ddd), 5.25 (1H, s, br), 2.58 (2H, dt), 1.56 (2H, t), 1.31 (8H, m), 0.88 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	3390, 2935, 2863, 1643, 1609, 1517, 1183, 1024, 961, 809, 676
MS *m/z*	228(M^+), 169, 156, 143(100%), 95

Step 2

Preparation of 2-(2,3-Difluoro-4-heptylphenoxy)acetaldehde dimethyl acetal

The title compound was prepared and purified in a similar manner to that described for the preparation of 2-(4-pentylphenoxy)acetaldehyde dimethal acetal in Example 25(1) using the quantities stated.

2,3-Difluoro-4-heptylphenol (5.8 g, 25.0 mmol), bromoacetaldehyde dimethyl acetal (5.1 g, 30.0 mmol), potassium carbonate (6.9 g, 50.0 mmol), potassium iodide (0.2 g, 1.3 mmol).

A colourless oil was obtained, which solidified on cooling to a waxy solid.

Yield 5.4 g (68%) bp 170 °C at 0.05 mmHg.

^{1}H NMR $CDCl_3/\delta$	6.81 (1H, ddd), 6.67 (1H, ddd), 4.72 (1H, t), 4.05 (2H, d), 3.47 (6H, s), 2.57 (2H,

	dt), 1.57 (2H, m), 1.29 (8H, m), 0.88 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2936, 2863, 1640, 1513, 1176, 1151, 1115, 1095
MS *m/z*	316(M^+), 284, 253, 126, 75(100%)

Step 3

Preparation of 6,7-Difluoro-5-heptylbenzo[b]furan

The title compound was prepared and purified in a similar manner to that described for the preparation of 5-bromobenzo[b]furan (Example 9(2)) using the quantities stated. The product of step 2 (5.4 g, 17.0 mmol), polyphosphoric acid (7.3 g).

A pale yellow liquid was obtained.

Yield 0.5 g (12%) bp 135 °C at 0.1 mmHg.

^{1}**H NMR** CD_2Cl_2/δ	7.65 (1H, d), 7.16 (1H, m), 6.76 (1H, dd), 2.72 (2H, dt), 1.63 (2H, qui), 1.31 (8H, m), 0.88 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2933, 2867, 1616, 1131, 1077, 926, 871, 763, 733, 551
MS *m/z*	252(M^+), 209, 167(100%), 153, 118

Step 4

Preparation of 6,7-Difluoro-5-heptylbenzo[b]furan-2-boronic acid

The title compound was prepared and purified in a similar manner to that described in Example 20(2) using the quantities stated.

The product of step 3 (0.5 g, 1.8 mmol), n-butyllithium (2.5M in hexanes, 0.8 ml, 2.0 mmol), trimethyl borate (0.4 g, 3.6 mmol).

An orange solid was obtained.

Yield 0.3 g (66%)

MS *m/z* 252(M^+), 180, 167(100%), 119, 57

Step 5

Preparation of 4-Bromo-3-fluoro-4'-pentylbiphenyl

The title compound was prepared and purified in a similar manner to that described in Example 24(1) using the quantities stated.

1-Bromo-2-fluoro-4-iodobenzene (6.4 g, 21.0 mmol), 4-pentylbenzeneboronic acid (Example 3(2)) (4.5 g, 23.0 mmol), sodium carbonate (5.6 g, 53.0 mmol), tetrakis(triphenylphosphine)palladium(0) (1.2 g, 1.0 mmol)

The product was further purified by distillation.

A pale-yellow liquid was obtained.

Yield 1.7 g (25%) (a quantity was lost through spillage) bp 190 °C at 0.04 mmHg.

^{1}**H NMR** CD_2Cl_2/δ	7.60 (1H, dd), 7.49 (2H, d), 7.37 (1H, dd), 7.29 (1H, dd), 7.28 (2H, d), 2.65 (2H, t), 1.64 (2H, qui), 1.35 (4H, m), 0.91 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2933, 2861, 1560, 1195, 1057, 875, 805, 547
MS *m/z*	322,320(M^+), 263, 250, 183(100%), 170

Step 6

Preparation of 2-(2-Fluoro-4'-pentylbiphenyl)-6,7-difluoro-5-heptylbenzo[b]furan (Compound 78)

The title compound was prepared and purified in a similar manner to that described for in Example 24(1) using the quantities stated.

Product of step 5 (03.5 g, 1.4 mmol), product of step 4 (0.3 g, 1.2 mmol), sodium carbonate (0.4 g, 3.5 mmol), tetrakis(triphenylphosphine)palladium(0) (0.1 g, 0.1 mmol)

Final purification was by preparative hplc (acetonitrile/chloroform 4:1).

A white solid was obtained.

Yield 0.04 g (7%). Purity (hplc) 99.2%.

^{1}**H NMR** CD_2Cl_2/δ	8.07 (1H, dd), 7.58 (2H, d), 7.55 (1H, dd), 7.45 (1H, dd), 7.30 (2H, d), 7.21-7.19 (1H, m), 7.19-7.17 (1H, m), 2.75 (2H, dt), 2.66 (2H, t), 1.68-1.64 (4H, m), 1.37-1.26 (12H, m), 0.91 (3H, t), 0.89 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2925, 2855, 1614, 1556, 1110, 1062, 915, 866, 800
MS *m/z*	492(M^+)(100%), 435, 407, 350, 175

Example 62

Preparation of Compound 1 in Table 1

Step 1

Preparation of 1-Bromo-4-octyloxybenzene

A mixture of *p*-bromophenol (40.0 g, 231 mmol), n-octyl bromide (50.2 g, 260 mmol), potassium carbonate (35.9 g, 260 mmol) and potassium iodide (2.2 g, 13 mmol)
in butanone (500 ml) was refluxed under nitrogen (48 h) and the reaction monitored by glc analysis. The mixture was filtered, and the solid washed with ether (2 x 300 ml). The filtrate was washed with sodium hydroxide (10%), followed by brine. The solvent was removed *in vacuo*, and the product purified by distillation.
A colourless liquid was obtained.

Yield 61.0 g (93%) bp 145 °C at 0.02 mmHg (lit.[3] 125°C).

^{1}**H NMR** $CDCl_3/\delta$	7.35 (2H, d), 6.76 (2H, d), 3.90 (2H, t), 1.76 (2H, qui), 1.35 (10H, m), 0.89 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2900, 1580, 1475, 1240, 1170, 1070, 820, 640, 500
MS *m/z*	286,284(M^+), 171(100%), 157, 143, 93

Step 2

Preparation of 2-methyl-4-(4-octyloxyphenyl) but-3-yn-2-ol

A mixture of compound the product of step 1 (61.0g, 214 mmol), tetrakis(triphenylphosphine)palladium(0) (2.4 g, 2.1 mmol), cuprous iodide (0.4 g, 2.1 mmol) and dry diisopropylamine (400 ml) was stirred under nitrogen (10 min).

2-Methyl-but-3-yn-2-ol (45.0 g, 535 mmol) in dry diisopropylamine (90 ml) was added dropwise, and the mixture was refluxed (4 h); the reaction progress was monitored by tlc analysis. When cool, water was added, and the mixture was filtered through a pad of 'Hyflo Supercel', washing the pad with ether. The separated aqueous layer was washed with ether (2 x 300 ml), and the combined organic layers washed with brine and dried ($MgSO_4$). After removal of the solvent *in vacuo*, the product was purified by flash chromatography [silica gel, petroleum fraction (bp 40-60 °C) (unreacted starting material), and DCM (product)].

A heavy brown oil was obtained

Yield 33.2 g (54%).

^{1}H NMR $CDCl_3/\delta$	7.33 (2H, d), 6.81 (2H, d), 3.93 (2H, t), 1.76 (2H, qui), 1.60 (6H, s), 1.28 (12H, m), 0.88 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	3440, 2880, 1600, 1505, 1465, 1370, 1245, 960, 835
MS *m/z*	288,286(M^+), 273, 175, 159, 43(100%)

Step 3

Preparation of 4-Octyloxyphenylacetylene

The product of step 2 (33.0 g, 115 mmol) and potassium hydroxide (7.1 g, 126 mmol) in toluene (250 ml), were refluxed with stirring under nitrogen (3.5 h), using a Dean and Stark apparatus. Tlc analysis indicated a complete reaction. The cooled reaction mixture was poured into water (150 ml) and the layers were separated. The aqueous phase was neutralised with hydrochloric acid (0.02 M) to pH 7, and washed with ether (3 x

100 ml). The combined organic layers were washed with brine and dried ($MgSO_4$). After removal of the solvent *in vacuo*, the residue was flash chromatographed [silica gel / petroleum fraction (bp 40-60 °C), DCM 1:1]. The product was then distilled *in vacuo*.
A pale-yellow liquid was obtained.

Yield 6.4 g (68%) bp 122 °C at 2.7 mmHg

^{1}**H NMR** $CDCl_3/\delta$	7.42 (2H, d), 6.82 (2H, d), 3.94 (2H, t), 3.00 (1H, s), 1.77 (2H, qui), 1.35 (10H, m), 0.88 (3, t)
IR (KBr) ν_{max}/cm^{-1}	3310, 3290, 2920, 2850, 2110, 1600, 1500, 830
MS *m/z*	230(M^+), 187, 145, 118(100%), 101

Step 4

Preparation of 4,6-Diiodoresorcinol

To resorcinol (5.0 g, 45 mmol) in hydrochloric acid (conc.) / water 14:11 v/v (185 ml), iodine monochloride (14.6 g, 90 mmol) was added with stirring under nitrogen. Stirring was continued (15 min), followed by addition of solid sodium sulphite until the iodine colouration was removed. The reaction mixture was filtered and the solid washed with cold water. The solid was then dried *in vacuo* (KOH) and recrystallized (CCl_4).
Colourless needles were obtained.

Yield 8.6 g (53%) mp 139-145 °C (lit.[4] 145°C).

^{1}**H NMR** DMSO-d^6/δ	9.55 (2H, s), 7.57 (1H, s), 6.53 (1H, s)
IR (KBr) ν_{max}/cm^{-1}	3455, 1565, 1285, 1150, 1030, 875, 630, 460
MS *m/z*	362(M^+), 235, 108, 79, 50(100%)

Step 5

Preparation of 4,6-Diiodoresorcinol dibenzoate ester

To a stirred mixture of compound the product of step 4 (15.0 g, 42 mmol) and benzoyl chloride (12.8 g, 91 mmol) in dry DCM

(150 ml), dry triethylamine (9.2 g, 91 mmol) was added dropwise with exclusion of moisture, and the mixture was then refluxed (2 h). When cool, the mixture was poured into water and washed with DCM (2 x 200 ml). The combined organic phases were washed with hydrochloric acid (0.1M) and water, and dried ($MgSO_4$). The solvent was removed *in vacuo* and the residue recrystallized (toluene).

White, fibrous crystals were obtained.

Yield 20.6 g (86%), mp 185-7 °C (lit.[4] 195-200°C (decomp.)).

^{1}H NMR $CDCl_3/\delta$	8.36 (1H, s), 8.26 (4H, d), 7.68 (2H, t), 7.54 (4H, t), 7.31 (1H, s)
IR (KBr) ν_{max}/cm^{-1}	1745, 1235, 1150, 1050, 700
MS *m/z*	570(M^+), 443, 127(100%), 105, 77

Step 6

Preparation of 2-(4-Octyloxyphenyl)-5-(4-octyloxyphenylethynyl)benzo[b]furan-6-benzoate ester (Compound 1)

The product of step 3 (0.7g, 3 mmol) was placed in a three-necked flask fitted with septum, condenser, thermometer and addition funnel. The apparatus was heated, evacuated, and flushed with nitrogen. Dry THF (10 ml), was added and the system degassed at -40 °C. The flask was flushed with nitrogen and n-butyllithium (1.4 ml, 3.5 mmol, 2.5M in hexanes) was added dropwise with stirring, maintaining the temperature below 0 °C. The mixture was stirred at this temperature (15 min), the system was cooled (-40 °C) and anhydrous zinc chloride (0.5 g, 3.5 mmol) in dry THF (20 ml) was added dropwise with stirring. The mixture was allowed to return to room temperature whilst stirring. The product of step 5 (0.7 g, 1.2 mmol) and tetrakis(triphenylphosphine)palladium(0) (0.1 g, 0.1 mmol) were added and the mixture refluxed with stirring under nitrogen. When tlc analysis indicated no further reaction (3 days), the mixture was allowed to cool. The solvent was

removed *in vacuo* and the residue triturated with ether, whence a white solid precipitated. The solid was then re-triturated with petroleum fraction (bp 40-60 °C) from solution in methanol, and finally recrystallized (ethanol). Pale yellow crystals were obtained.

Yield 0.1 g (14%). Purity (hplc) >98%.

^{1}**H NMR** $CDCl_3/\delta$	8.34 (2H, d), 7.77 (2H, d), 7.74 (1H, s), 7.67 (1H, t), 7.53 (2H, t), 7.47 (1H, s), 7.09 (2H,d), 6.97 (2H, d), 6.86 (1H, d), 6.69 (2H, d), 4.20 (2H, t) 3.90 (2H, t), 1.78 (4H, m), 1.30 (20H, m), 0.89 (3H, t), 0.88 (3H, t)
IR (KBr) ν_{max}/cm^{-1}	2920, 2850, 1735, 1500, 830
MS *m/z*	671(M^+), 566, 446, 341, 105(100%)

Example 63

Liquid Crystal Properties

The liquid crystal properties of the compounds of the invention were tested using conventional methods. Examples of transitions are provided above in the Examples. However, the results are summarised in Table 3.

Table 3

Compound No.	Transition Temp °C	Enthalpy/Jg^{-1}
1	K 87.1 N 150.5 Iso	
2	K 39 [36.8SmA] Iso	
3	K 31.1 N 60.5 Iso	67.3 1.8
4	K 132 SmA 184.1 Iso	
5	K 76 SmA 140.9 N 144.4 Iso	
6	K 118 SmA 151.9 Iso	
7	K 103 SmA 158 N 178.4 Iso	
8	K 95.4 SmA 158 N 170 Iso	
9	K 78.5 SmA 146.2 N Iso	

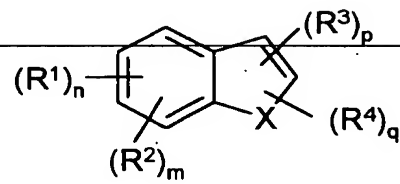
Compound No.	Transition Temp °C	Enthalpy/Jg^{-1}
10	K 98.7 SmA 152.2 Iso	
11	K 75.8 SmA 123.2 (TGBA*) N* 133.2 (BPI-III) Iso	
12	K 103 SmA 119.7 Iso	68.8 2.3
13	K 101 SmI/F 104.5 SmA 114.9 Iso	
14	K 86.5 N 87.5 Iso	69.1 -1.1 (cooling)
15	K 129.5 SmA 180 N 186 Iso	
16	K 62 SmA 87 N 97 Iso	83.4 0.3 1.3
17	K 40 SmA 44.5 N 48.5 Iso	
18	K 104.5 SmA 183.5 N 194 Iso	
19	K 104 SmA 182.5 N 185 Iso	
20	K 120 SmA 193 N 214.5 Iso	
21	K 106.5 SmA 188.5 N 203.5 Iso	
22	K 110.5 SmA 161.5 N* 172.5 BPI 173.5 Iso	
23	K 14 SmA 247 Iso	
24	K [51 SmA] 76 Iso	
25	K 58 [48.9 N] Iso	97.1 -0.6 (cooling)
26	K 51.1 N 56.4 Iso	97.7 0.6
27	K 99.7 [86.5 N] Iso	93.9 -1.2 (cooling)
28	K 147.3 [134 B] N 255.6 Iso	66.1 -0.4 (cooling) 1.6
29	K 187.1 N 284.2 Iso	35.5 2.2
30	K 134 SmA 186.8 N 191.4 Iso	
31	K 90.9 SmC 97.1 SmA 134 N 143.1 Iso	
32	K 70.1 SmC 100.7 SmA 109.1 N 142.6 Iso	

Compound No.	Transition Temp °C	Enthalpy/Jg^{-1}
33	K 145.9 SmA 184.5 Iso	
34	K 28.1 SmA 49.6 N 60 Iso	49.5 0.2 1.7
35	K 139 N 252.6 Iso	79.0 1.2
36	K 28.2 SmA 34.3 N 48.8 Iso	58.9 0.2 0.7
37	K 107.9 N 148.4 Iso	
38	K 74 N 119.7 Iso	
39	K 89.8 N 94.6 Iso	
40	K 24.5 N 45.2 Iso	9.3 0.6
41	K 77.6 (N 58.5) Iso.	91.6 -1.6 (cooling)
42	K 98.0 Iso	
43	K 200.3 SmC 255.8 Iso	
45	K 151.5 SmA 152.0 Iso	
46	K 172 SmC 193.2 N 253.7 Iso	
47	K 225 N 235 Iso	
48	K 43.0 (30.9N) Iso	
50	K 133.8 N 230.5 Iso	51.3 0.7
51	K150.8 B167.0 N 280.3 Iso	31.8 30.1 1.9
52	K 94/8 n 236.7 Iso	81.4 1.5
53	K 183 N 299 Iso	
54	K 86.5 N 87.5 Iso	
55	K 113.0 n 240.7 Iso	64.5 2.1
57	K 96.4 SmA 144.3 N 145.8 Iso	
58	K 63.0 SmA 134.3 Iso	
59	K 81.7 (71.7 N) Iso	
62	K 76.0 SmA 140.9 N 144.4 Iso.	
64	K 103.0 SmA 158.0 N 178.4 Iso.	
65	K 95.4 SmA 158.0 N 170.0 Iso.	
66	K 78.5 SmA 146.2 N 155.0 Iso.	
67	K 75.8 SmA 122.5 TGBA* 123.2 N* 130.8 BPI-III 133.2 Iso.	
68	K 9.7 Iso (Recryst. 0.1 °C).	
69	K 76.0 (51.0 SmA) Iso.	

Compound No.	Transition Temp °C	Enthalpy/Jg^{-1}
70	K 104.5 SmA 183.5 N 194.0 Iso.	
71	K 90.0 SmA 100.5 Iso.	
72	K 104.0 SmA 182.5 N 185.0 Iso.	
73	K 120.0 SmA 193.0 N 214.5 Iso.	
74	K 106.5 SmA 188.5 N 203.5 Iso.	
76	K 110.5 SmA 161.5 N* 172.5 BPI 173.5 Iso.	
77	K 14.0 SmA 27.0 Iso.	
78	K 132.0 SmA 184.1 Iso.	
79	K 129.5 SmA 180.0 N 186.0 Iso.	
80	K 118.0 SmA 151.9 Iso.	
81	K 96.4 SmA 144.3 N 145.8 Iso.	
82	K 70.1 SmC 100.7 SmA 109.1 N 142.6 Iso.	
83	K 40.0 SmA 44.5 N 48.5 Iso.	
84	K 77.6 SmA 103.4 Iso.	
85	K 134.0 SmA 186.8 N 191.4 Iso.	
86	K 90.9 SmC 97.1 SmA 134.0 N 143.1 Iso.	
87	K 107.9 SmA 148.4 Iso.	
88	K 74.0 N 119.7 Iso.	
89	K 89.8 N 94.6 Iso.	
90	K 81.7 (N 71.7) Iso.	
91	K 63.0 SmA 134.3 Iso.	
92	K 87.1 N 150.0 Iso.	
102	K 93.2 Iso	56.5

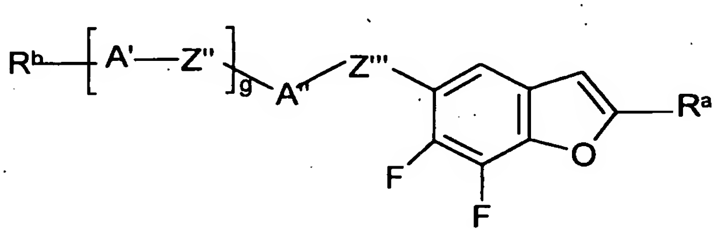
Claims

1. A liquid crystal compound of general formula (I)



(I)

where X is O, S or Se, each R^1 and R^3 are independently selected from cyano, halo, optionally substituted hydrocarbyl, optionally substituted alkoxy, optionally substituted heterocyclyl or carboxy or a hydrocarbyl ester or amide thereof, provided that at least one or group R^1 or R^3 is other than cyano or halo, each R^2 and R^4 is independently selected from halo, nitro, lower alkyl optionally substituted by halo, or a group $R^aC(O)O-$ where R^a is optionally substituted hydrocarbyl, n is 1 or 2, m is 0, 1, 2 or 3, p is 1 or 2 and q is 0 or 1, provided n + m do not exceed 4 and p = q do not exceed 2, and further provided that the compounds are other than a compound of formula (A) or (B)



(A)

where R^a is a C_{1-8} alkyl group; R^b is H, or a C_{1-12}alkyl or C_{2-12}alkenyl group, either of which may be optionally substituted by one CN or CF_3 group or one or more halogen atoms; and wherein one or more $-CH_2-$groups in the

alkyl or alkenyl groups is optionally replaced by -O-, -S-, -C(O)-, C(O)O-, -OC(O)- or -OC(O)O- provided that oxygen and sulphur atoms are not directly linked to each other;

A′ and A′′ are indepedently selected from:

a) a trans-1,4-cyclohexylene residue in which one or more non-adjacent CH_2 groups can be replaced by -O- and/or -S-;

b) a 1,4-cyclohexenyl residue;

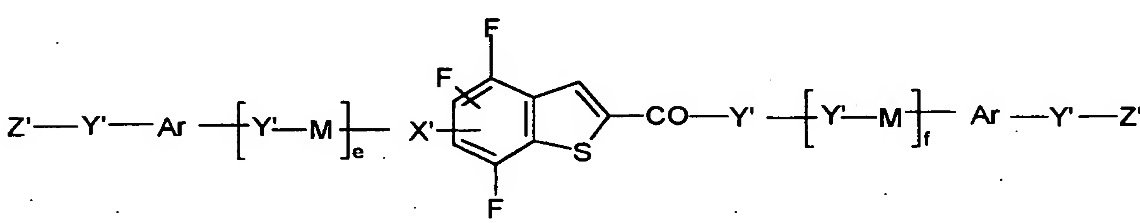
c) a 1,4-phenylene residue in which one or two CH groups can be replaced by N;

d) a residue from the group 1,4-bicyclo(2,2,2)-octylene, piperidine-1,4-diyl, naphthalene-2,6-diyl, decahydronaphthalene-2,6-diyl and 1,2,3,4-tetra-hydronaphtahlene-2,6-diyl;

whereby residues a), b) and c) can be substituted by CN, Cl, or F,

Z′ and Z′′ independently represent -C(O)O-, -OC(O)-, $-CH_2O-$, $-OCH_2-$, $-CH_2CH_2-$, -CH=CH-, -C≡C- or a single bond and

g is 0,1 or 2



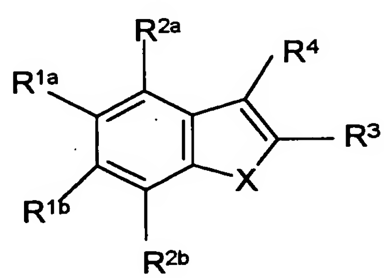
(B)

where

each Ar is a bond or a spacer group such as a C_{2-30}alkylene or C_{2-30}alkenylene group, optionally substituted with C_{1-4}alkyl, fluoro, chloro, bromo, cyano, or hydroxy, and optionally interposed with one or more -O-, -S-, -NH-, $-NR^c-$, -COO-, OCO, OCOO or CO;

each M is independently selected from optionally substituted aliphatic, aromatic, heteroaliphatic or a heteroaromatic ring system,
X′ is O, S, COO, OCOO, CONH or $CONR^c$ where R^c is C_{1-4}alkyl;
e and f are independently selected from 0,1 or 2,
each Y′ group is independently selected from O, S, COO, OCO, OCOO, CONH, NHCO, $CONR^c$, or NR^cCO where R^c is as defined above;
each Z′ group is independently selected from hydrogen, cyano or a polymerisable group.

2. A liquid crystal compound according to claim 1 which is of general formula (IA)



(IA)

where X is as defined in claim 1,
R^{1a} and R^{1b} are independently selected from hydrogen, cyano, halo, optionally substituted hydrocarbyl, optionally substituted heterocyclyl or carboxy or a hydrocarbyl ester or amide thereof, provided that at least one group R^{1a} or R^{1b} is other than hydrogen;
one of R^3 or R^4 is cyano, halo, optionally substituted hydrocarbyl, optionally substituted heterocyclyl or carboxy or a hydrocarbyl ester or amide thereof, and the other is hydrogen, halo, nitro, lower alkyl optionally substituted by halo, or a group $R^aC(O)O-$ where R^a is optionally substituted hydrocarbyl;

R^{2a} and R^{2b} are independently selected from hydrogen, halo, nitro, lower alkyl optionally substituted by halo, or a group $R^bC(O)O-$ where R^b is optionally substituted hydrocarbyl.

subject to the further provisos that:
(i) at least one group R^{1a} or R^{1b} or R^3 or R^4 is other than cyano or halo;
(ii) where X is S, R^3 is carboxy or a hydrocarbyl ester or amide thereof, R^4 is hydrogen, R^{2a} and R^{2b} are not both fluoro;
(iii) where X is O, R^1 is an optionally substituted hydrocarbyl or carboxy or a hydrocarbyl ester or amide thereof, R^2 is hydrogen, and R^{1b} and R^{2b} are both fluorine, then R^3 is other than C_{1-8} alkyl.

3. A liquid crystal compound according to claim 2 wherein R^{2a} is hydrogen.

4. A liquid crystal compound according to claim 2 or claim 3 wherein at least one of R^{1b}, R^{2b} or R^4 is fluoro.

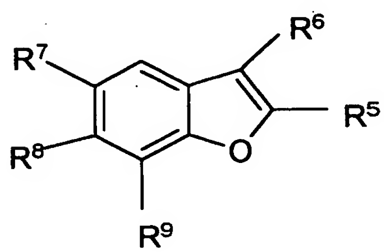
5. A liquid crystal compound according to any one of claims 2 to 4 wherein one of R^{1b} or R^{1a} or R^3 or R^4 is cyano or halo and the other is optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, an optionally substituted aryl, optionally substituted heterocyclyl, carboxy or a hydrocarbyl ester thereof.

6. A liquid crystal compound according to any one of the preceding claims where R^3 is cyano, halo, optionally substituted hydrocarbyl, optionally substituted heterocyclyl or carboxy or a hydrocarbyl ester or amide thereof, and R^4 is hydrogen, halo, nitro, lower alkyl optionally substituted by halo, or a group $R^aC(O)O-$ where R^a is optionally substituted hydrocarbyl.

7. A liquid crystal compound according to any one of the preceding claims 1 to 5 where X is oxygen.

8. A liquid crystal compound according to claim 6 where the compound of formula (I) is a compound according to claim 2 and where R^{1a} and R^{2a} are not both fluorine.

9. A liquid crystal compound according to claim 1 which comprises a compound of formula (II)



(II)

wherein R^5 is cyano, halo, optionally substituted hydrocarbyl, optionally substituted heterocyclyl or carboxy or a hydrocarbyl ester or amide thereof,
one of R^7 and R^8 is a cyano, halo, optionally substituted hydrocarbyl, optionally substituted heterocyclyl or carboxy or a hydrocarbyl ester or amide thereof and the other is hydrogen, cyano, halo, optionally substituted hydrocarbyl, optionally substituted heterocyclyl or carboxy or a hydrocarbyl ester or amide thereof;
R^6 is hydrogen, cyano or fluoro, and
R^9 is hydrogen, cyano or fluoro,
provided that where R^5 is cyano or fluoro, at least one of R^7 or R^8 is optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted alkoxy, optionally substituted aryl, optionally substituted heterocyclyl, carboxy or an ester thereof; and where one of R^7 or R^8 is cyano or fluoro and the other is hydrogen, R^5 is

optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted alkoxy, optionally substituted aryl, optionally substituted heterocyclyl, carboxy or an ester thereof.

10. A liquid crystal compound according to claim 9 which comprises a compound of formula (II) where R^6 is hydrogen or fluoro, and R^9 is hydrogen or fluoro.

11. A liquid crystal mixture comprising a compound according to any one of the preceding claims.

12. A liquid crystal mixture according to claim 11 which comprises at least two different compounds according to any one of claims 1 to 10.

13. A liquid crystal device such as a liquid crystal display device (LCD) comprising a compound according to any one of claims 1 to 10 or a mixture according to claim 11 or claim 12.

14. A liquid crystal compound according to any one of claims 1 to 10 or a mixture according to claim 11 or claim 12, which has electroclinic properties.

15. An electroclinic device comprising a liquid crystal compound or a mixture according to claim 14.

16. A liquid crystal compound according to any one of claims 1 to 10 or a mixture according to claim 11 or claim 12, which has cholesteric properties.

17. A device comprising a liquid crystal compound or a mixture according to claim 16, wherein said device is a thermoptic, thermographic or electro-optical device.

18. A liquid crystal compound according to any one of claims 1 to 10 or a mixture according to claim 11 or claim 12, which has ferroelectric properties.

19. A ferroelectric device comprising a liquid crystal compound or a mixture according to claim 18.

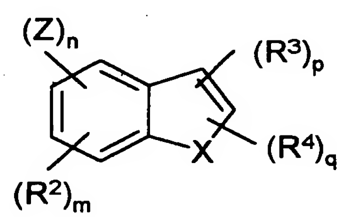
20. A liquid crystal compound according to any one of claims 1 to 10 or a mixture according to claim 11 or claim 12, which has flexo-electric properties.

21. A flexo-electric device comprising a liquid crystal compound or a mixture according to claim 20.

22. A liquid crystal compound according to any one of claims 1 to 10 or a mixture according to claim 11 or claim 12, which has pyro-electric properties.

23. A pyro-electric device comprising a liquid crystal compound or a mixture according to claim 22.

24. A method of preparing a compound of formula (I) which comprises either (i) reacting a compound of formula (III)



(III)

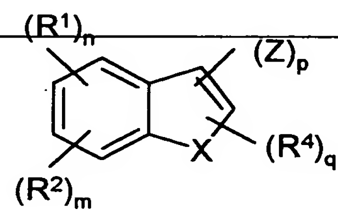
where R^2, R^3, R^4, X, n, m, p and q are as defined in relation to formula (I), and Z is either a leaving group or a group $B(OH)_2$, with a compound of formula (IV)

R^1-Z'

(IV)

where R^1 is as defined in relation to formula (I) and Z′ is a group $B(OH)_2$ where Z is a leaving group, or a leaving group where Z is a group $B(OH)_2$; or

(ii) reacting a compound of formula (V)



(V)

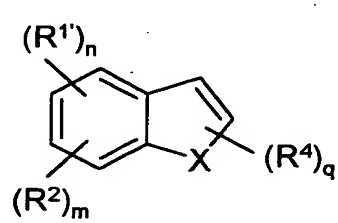
where R^1, R^2,R^4, X, n, m, p and q are as defined in relation to formula (I), and Z is as defined in relation to formula (III), with a compound of formula (VI)

$$R^3\text{–}Z'$$

(VI)

where R^3 is as defined in relation to formula (I) and Z′ is as defined in relation to formula (IV), or

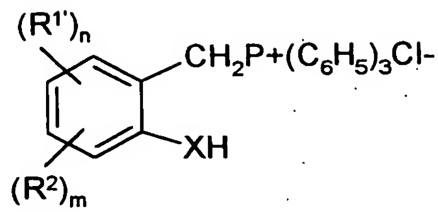
(iii) where q is 0 and p is 1 and R^3 is a carboxy group, carboxylating a compound of formula (IX)



(IX)

were R^2, R^4, X, m,n and q are as defined in relation to formula (I), and $R^{1'}$ is a group R^1 as defined in relation to formula (I) or a precursor thereof; with a carboxylating agent, and thereafter acidifying the product with an acid such as glacial acetic acid, or

(IV) where q is 0, reacting a compound of formula (XIII)



(XIII)

where $R^{1'}$, R^2, X, n and m are as defined above, with a compound of formula (XIV)

$$HO_2C-R^{3'}$$

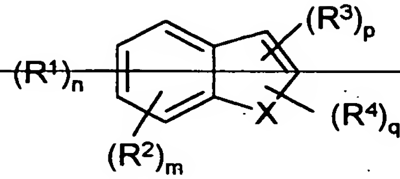
(XIV)

where $R^{3'}$ is a group R^3 as defined in relation to formula (I) or a precursor thereof;

and thereafter, if necessary, changing any groups R^1, R^2 R^3 or R^4 to different such groups.

Abstract

A liquid crystal compound of general formula (I)



(I)

where X is O, S or Se, and R^1, R^2, R^3, R^4, m, n, p and q are as specified in the application.

Liquid crystal devices comprising said compounds are also claimed.